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BULLETIN

OF THE NEW YORK ACADEMY OF MEDICINE

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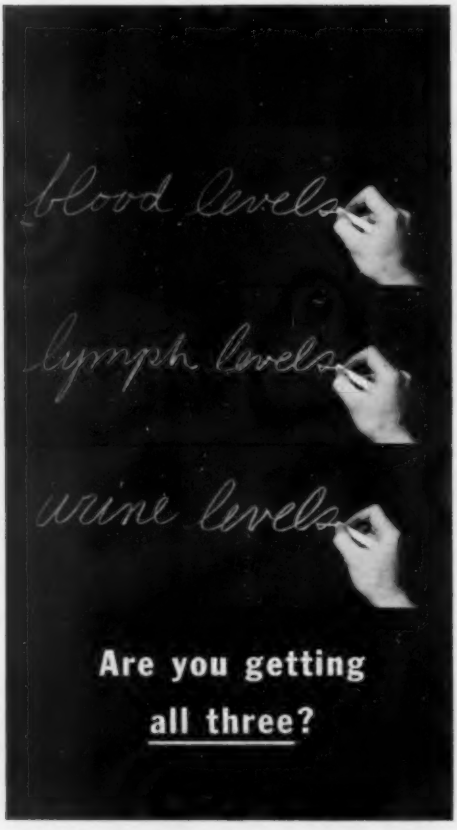

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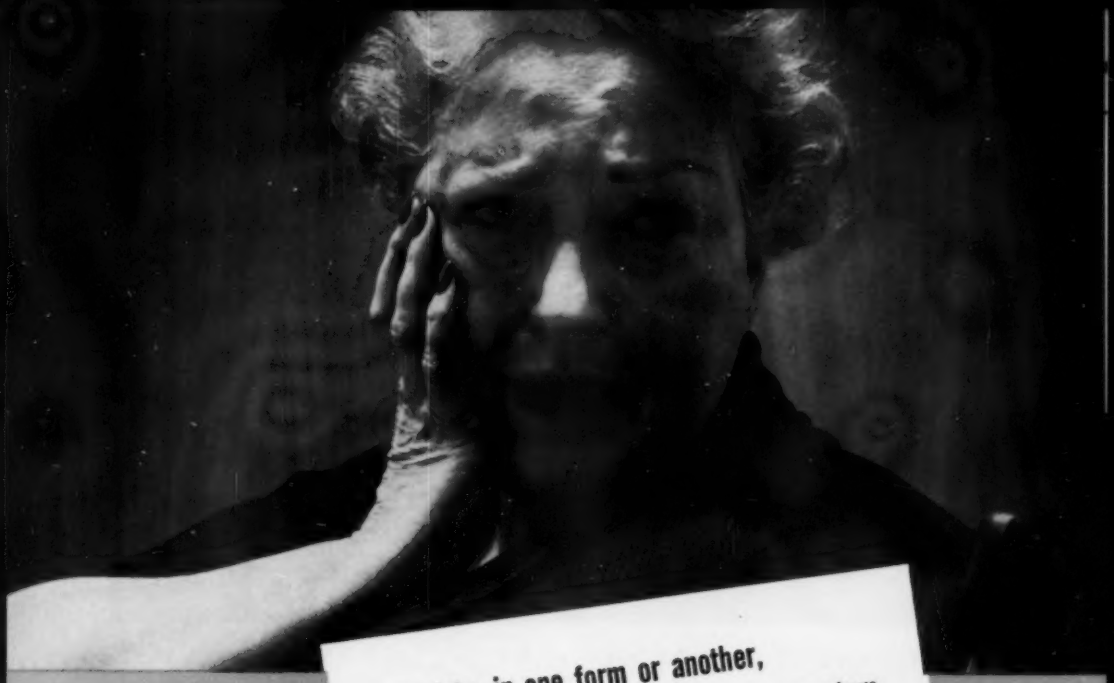

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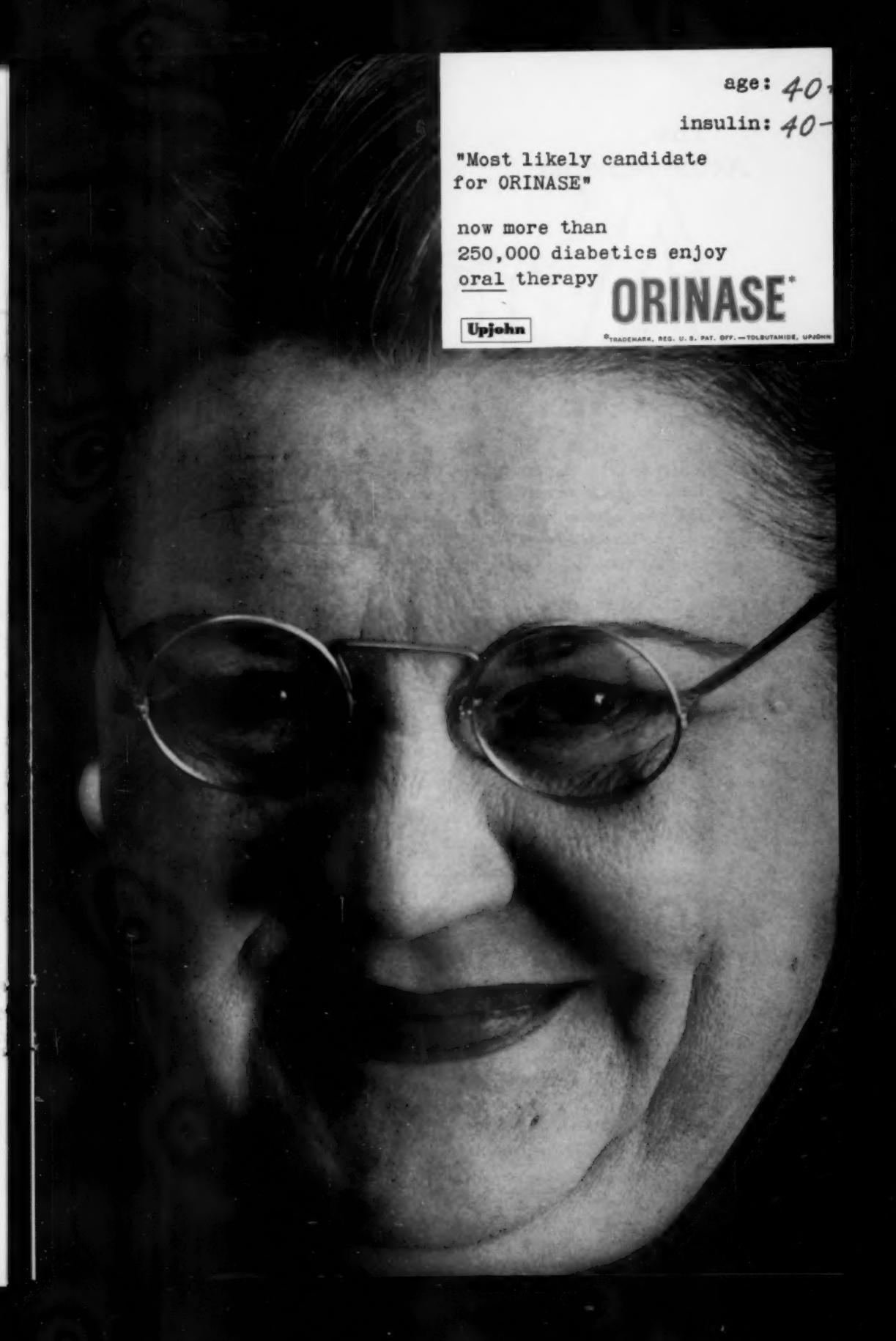
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2. Shelley, W. B., and Pillsbury, D. M.: Personal Communication.
3. Sherwood, A., and Cooke, R. A.: Personal Communication.
4. Freyberg, R. H., Berntsen, C. A., and Hellman, L.: Paper presented at International Congress on Rheumatic Diseases, Toronto, June 25, 1957.
5. Hartung, E. F.: Personal Communication.
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10. Barach, A. L.: Personal Communication.
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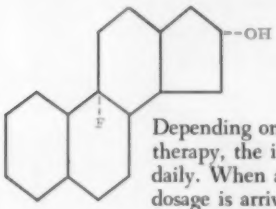

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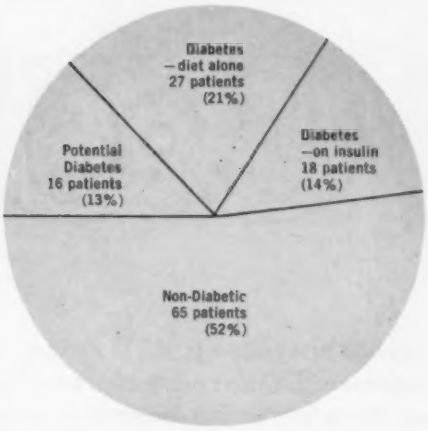

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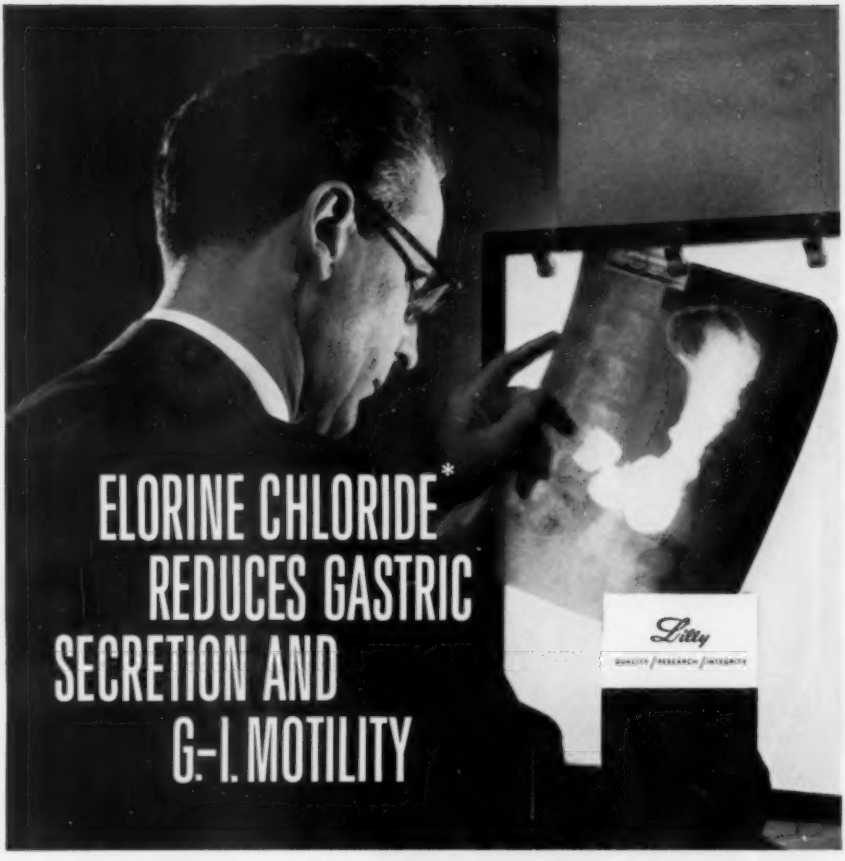

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1. Sun, D. C. H., and Shay, H.: A.M.A. Arch. Int. Med., 97:442, 1956.

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AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

ROBERT L. CRAIG, *Editor*

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BULLETIN OF
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VOL. 34, NO. 5 MAY 1958

RENAL REGULATION OF URIC ACID EXCRETION IN NORMAL AND GOUTY MAN: MODIFICATION BY URICOSURIC AGENTS*

ALEXANDER B. GUTMAN

Director, Department of Medicine, The Mount Sinai Hospital; Professor of Medicine, College of Physicians and Surgeons, Columbia University

and

T'SAI FAN YÜ

Research Associate in Medicine, The Mount Sinai Hospital; Associate in Medicine, College of Physicans and Surgeons, Columbia University

THERE has been a recent resurgence of interest in the mechanisms of renal regulation of uric acid excretion in man, and the effects thereon of drugs, notably of uricosuric agents. The present study is an attempt to summarize the salient points brought out by investigations in this area during the past several years.

Current concepts of the renal regulation of uric acid excretion in normal man. The prevailing view[1], briefly stated, is that in normal

* From the Departments of Medicine, The Mount Sinai Hospital, and Columbia University, College of Physicians and Surgeons, New York, New York.
Presented at the Postgraduate Week on *Research Contributions to Clinical Practice*, at The New York Academy of Medicine, October 10, 1957.
The work reported was supported by a grant-in-aid (A-162) from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, U.S. Public Health Service, and a grant from the Arthritis and Rheumatism Foundation, New York State Chapter.

man the plasma urate is wholly filtrable at the glomerulus[2]; the filtered urate is reabsorbed (presumably in the proximal convolution) to the extent of 90-95 per cent of the load presented to the tubules; and the urate excreted in the urine represents that 5-10 per cent of the filtered load which has escaped reabsorption. In quantitative terms, at a glomerular filtration rate of 120 ml/min., with a mean plasma urate of 5.6 per cent for normal adult males, and assuming complete filtrability of the plasma urate at the glomerulus, urate would be delivered to the glomerular filtrate at a rate of 6.7 mg./min. In normal adult males, UV_{urate} approximates a mean of 0.5 mg./min. There is, then, a mean deficit of 6.2 mg./min. or 92.5 per cent of the filtered urate, which is attributed to tubular reabsorption.

The work of Berliner and associates[3] indicates that reabsorption of urate in the tubules is an "active", presumably enzymatic, process of limited capacity, with a Tm of the order of 15 mg. urate/min. The nature of this transport mechanism has not been further defined. Nor has the nature of the proximate mechanism regulating renal excretion of urate been clarified, since, for reasons that are quite obscure, urate is excreted in the urine at filtered urate loads far below the tubular capacity for reabsorption of urate.

Current concepts of the renal regulation of uric acid excretion in gouty man. So far as has been determined, the plasma urate in the hyperuricemia of gout also is completely filtrable[2] and the renal regulation of uric acid excretion in gouty subjects does not differ in any essential from that of normal man. The quantitative relationships, however, are different, as indicated by the results of clearance studies, using standard techniques, made in 150 gouty subjects[4].

In gouty subjects, the glomerular filtration rate, as measured by the inulin clearance, usually is below the commonly accepted mean normal figure for men of 125 ml/min/1.73 sq. m. body surface[1, 4]. When compared with non-gouty subjects of equivalent age[5], however, the differences in distribution are not statistically significant[4]. The decline in filtration rate would thus appear to be ascribable for the most part not to gout per se but to vascular changes related to aging. Our data[4] do indicate a statistically significant reduction in renal plasma flow, as measured by the clearance of para-aminohippurate, when compared with non-gouty subjects of comparable age[5].

Since the filtration rate is relatively well maintained in relation to

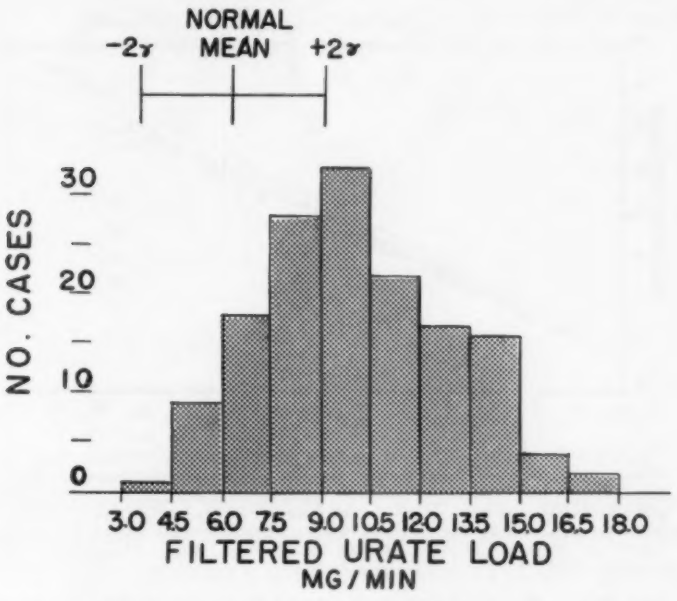

Fig. 1.—Distribution of filtered urate loads (C_{inulin} x P_{urate}) in 150 gouty subjects. The normal mean ± 2 sigmas is indicated.

age in most patients with gout, and the plasma urate is distinctly elevated (mean, 9.0 ± 1.4 mg. per cent in the 150 patients in question), it follows that the filtered urate load, calculated as the product of these two quantities, should be abnormally large. Figure 1, showing the distribution of the estimated filtered urate loads in 150 gouty subjects, fulfills this expectation. The mean was found to be 10.1 mg./min., about 50 per cent above the normal mean; and in some cases the filtered urate was more than twice the normal mean. For reasons indicated elsewhere[4], this increase is taken to be a reflection of over-production of uric acid in the gouty subjects in question.

The increase in filtered urate load occurring in most gouty subjects has interesting consequences in relation to the magnitude of the urate reabsorbed by the tubules, as calculated by the difference between the filtered and excreted urate. These alterations are best understood in the light of experiments by Berliner and associates[3], in which the filtered urate load in normal man was artificially increased by sustained

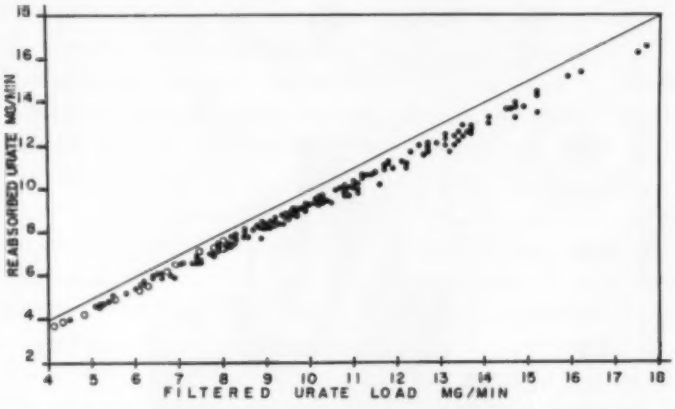

Fig. 2.—Relation of reabsorbed urate, mg/min., to filtered urate load in 12 non-gouty subjects (open circles) and 150 gouty patients (heavy circles). The diagonal line represents 100 per cent tubular reabsorption. Reabsorbed urate was calculated as the differences between filtered urate and UVurate, assuming no tubular excretion of urate. From Gutman and Yü, in the American Journal of Medicine 23:600-22, Oct. 1957. (Reprinted by permission.)

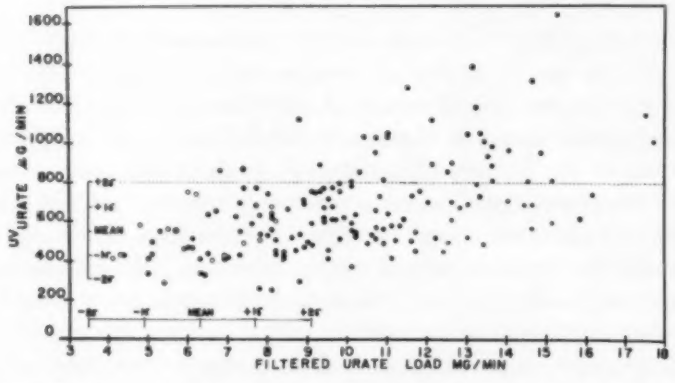

Fig. 3.—Relation of UV_{urate} to filtered urate load in 12 non-gouty subjects (open circles) and 150 gouty patients (solid dots). The normal means ± 2 sigmas are indicated. The broken line at 800 μg/min. indicates the normal mean UV_{urate} +2 standard deviations of distribution. From Gutman and Yü, in the American Journal of Medicine 23:600-22, Oct. 1957. (Reprinted by permission.)

TABLE I.—RELATION OF C_{INULIN} TO UV_{URATE} IN 150 GOUTY SUBJECTS

C_{inulin}* (ml/min.)	No. Cases	UV*urate* (μg/min.) 245—349	350—499	500—649	650—799	800—949	950—1099	1100—1249	1250—1399	1400—1657
50- 69	5		3	2						
70- 89	31	5	8	10	7			1		
90-109	32	2	8	8	8	1	4		1	
110-129	41		10	14	7	4	2	1	2	1
130-149	27		1	6	10	4	5	1		
150-179	14		1	5	4	2	1	1		
Total	150	7	31	45	36	11	12	4	3	1

* Not corrected to standard body surface area.

intravenous injection of uric acid. Under these circumstances the quantity of urate reabsorbed by the tubules steadily increased until the tubular capacity for urate reabsorption was saturated. This phenomenon is observed also in gouty subjects[4], the magnitude of reabsorbed urate increasing with the filtered urate load without, however, reaching a manifest Tm in the cases studied (Fig. 2). It is of interest that no (statistically) significant difference between gouty and normal subjects was noted in the percentage of filtered urate which was reabsorbed. Our data fail to give any indication of an intrinsic tubular defect in the kidneys of gouty subjects—excessive tubular reabsorption of urate beyond that of a normal response to increased filtered urate loads—which can be construed to be the primary cause of the hyperuricemia of gout.

In contrast to the regular relationship of reabsorbed urate to the filtered urate load, the quantity of urate excreted in the urine of gouty subjects is quite independent of the rate at which urate is filtered at the glomerulus (Fig. 3). The data indicate that an abnormally high UV_{urate} occurs much more frequently in association with abnormally large filtered urate loads but this seems to be a function of the elevation in plasma urate level rather than of the rate of glomerular filtration. In patients with well preserved filtration rates (C_{inulin} greater than 100 ml./min.) UV_{urate} unpredictably may be excessive, within the normal range, or occasionally less than the normal (Table I).

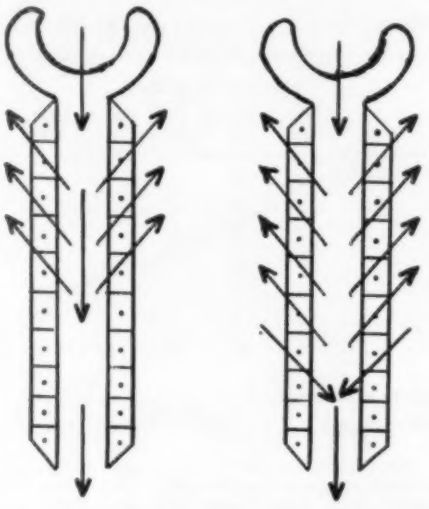

Fig. 4.—Schematic representation of two postulations of renal regulation of uric acid excretion in man. On the left, the plasma urate is pictured as virtually wholly filtrable at the glomerulus, the filtered urate is largely but not completely reabsorbed in passage through the tubules, and the excreted urate represents that small fraction of the filtered urate which has escaped reabsorption. On the right, the plasma urate again is pictured as virtually wholly filtrable at the glomerulus, the filtered urate is completely reabsorbed in the tubules, and the urate appearing in the urine is excreted by the tubules.

The question of tubular excretion of urate in man. This striking dissociation of the rate of urinary urate excretion from the other parameters of renal function, over the wide range of variation observed in patients with gout and/or intrinsic renal disease, was apparent to Garrod[6] and many subsequent investigators. An independent mechanism for renal excretion of urate in man, a tubular excretory system, has been proposed at various times. At first this was postulated on the general grounds of the Heidenhain theory of tubular excretion; Brøchner-Mortensen[7] has commented upon the insufficiency of evidence on this point. Later, when the disparity between the glomerular filtration rate and uric acid clearance in man became evident, it was postulated that the plasma urate was largely or wholly non-filtrable at the glomerulus[8-10] because of presumed protein-binding or occurrence as macromolecular uric acid polymers. These assumptions appear not to be tenable[2]. However, the available data seem to be consistent with an alternative hypo-

thesis[4], that the plasma urate is completely filtrable at the glomerulus, the filtered urate is wholly, or virtually wholly, reabsorbed by the tubules, and the urate excreted in the urine is derived, under ordinary circumstances, entirely or in very large part by tubular secretion (Fig. 4). (The renal regulation of urate excretion would thus be analogous, in principle to that of potassium; the postulation of tubular excretion of potassium has been supported by substantial evidence[11, 12].) Under certain circumstances, a substantial proportion of the excreted urate would include filtered urate which has escaped reabsorption; for example, when tubular reabsorption of urate is deficient because of inborn or acquired tubular defects or as a result of suppression by uricosuric drugs. This would occur also should the filtered urate loads exceed the capacity of the normal tubules fully to absorb them.

Tubular excretion of urate occurs in birds and reptiles (evidence reviewed by Smith[1]). In the mammalia, tubular excretion of urate has been demonstrated in the rabbit after infusion of uric acid[13] and in the Dalmatian coach hound[14] which has a genetically transmitted renal tubular defect in urate reabsorption. Tubular secretion of urate has been reported to occur in an apparently normal young man with defective tubular reabsorptive mechanisms of unknown nature[15].

Effect of drugs on tubular reabsorption (and tubular excretion?) of urate. It has been known for many years that salicylate in large dosage (5 gm.) is uricosuric whereas smaller doses of one or two grams cause retention of uric acid. A similar dual action has been noted with phenylbutazone and other uricosuric agents[16]. These paradoxical effects occur without any change in the filtration rate or filtrability of the plasma urate. It is conceivable that these drugs first enhance, then suppress one or more mechanisms for tubular reabsorption of urate; it is also possible, however, that in low dosage they inhibit tubular excretion of urate and in larger dosage also inhibit the tubular transport system responsible for reabsorption of urate. A similar multiple system explanation might be advanced for the puzzling fact that relatively small doses of salicylate can largely counteract the uricosuric properties of probenecid[17].

Pyrazinoic acid, as the free acid or amide, profoundly reduces the elimination of uric acid by the kidneys, to 5 or 10 per cent of the premedication figure, without lowering the inulin clearance[18]. Here again it is not known whether urate is retained because of suppressed tubular

excretion or enhanced tubular reabsorption; if the former, the degree of urate retention would make it necessary to postulate virtually complete tubular reabsorption of urate and tubular secretion of all or almost all the excreted urate. Administration of large doses of sodium lactate likewise results in striking urate retention, without decline in the inulin clearance[19]; the significance of this long known phenomenon also remains to be clarified.

The enhancement of urinary uric acid excretion produced by uricosuric drugs in appropriate dosage is attributable, it is generally agreed, to suppression of tubular reabsorption of urate. This has been shown for cinchophen[20], salicylate[21], probenecid[22], phenylbutazone[23] and the phenylbutazone analogs G-25671[24] and its sulfoxide metabolite, G-28315[25].

Application of uricosuric agents to the prevention and treatment of tophaceous deposits in gout. By protracted use of suitable uricosuric agents in gouty subjects it is possible to maintain the rate of urinary excretion of urate at levels greater than the rate of urate production (i.e., negative urate balance). By this device the urate of the extracellular fluid can be sustained at concentrations low enough to reverse the flow of urate into the tissues, with reduction of the body pool of urate, including solid deposits. Thus it was shown in 1951[26] that tophaceous deposits can be mobilized, and the further deposition of uric acid prevented. Since our report in 1951, 82 patients with tophaceous gout have been treated with uricosuric drugs—probenecid, G-25671, G-28315, salicylate—over periods from 6 months to 7 years[27, 28]. Once the uricosuric regimen was established, no new tophi appeared. Of the tophi present, in 36 cases (44 per cent) they disappeared completely or were markedly reduced in size; in 31 cases (38 per cent) the reduction was only moderate or slight; in 15 cases (18 per cent), for the most part under treatment for less than one year, there has been no apparent change in the size of the tophaceous deposits.

Chronic gouty arthritis, with impaired function of one or more joints, was present in 52 of these patients. In 37 cases (71 per cent) it was possible to achieve complete restoration of joint motion, in 12 (23 per cent) improvement was moderate to marked. Of 52 patients with chronic joint pain, 47 (90 per cent) were completely relieved, 3 (6 per cent) were somewhat improved.

In some cases failure was due to insufficient uricosuric response

because of impaired renal function, inadequate drug dosage (intolerance, renal colic) or immoderation in diet. In a few instances a satisfactory uricosuric response was obtained and some tophi disappeared but others proved to be refractory; evidently some tophaceous deposits (as it happens, the minority) are not accessible to humoral agents.

Summary

According to the prevailing view, the plasma urate in normal and gouty man is virtually wholly filtrable at the glomerulus; some 90-95 per cent of the filtered urate is reabsorbed in the tubules; and the urate excreted in the urine represents that 5-10 per cent of the filtered urate load which has escaped tubular reabsorption.

An alternative possibility is suggested, that the completely filtrable urate is wholly or virtually wholly reabsorbed by the tubules, and that the urate excreted in the urine in normal and gouty man ordinarily is derived entirely or in large part by tubular secretion.

Clearance techniques fail to disclose any primary, intrinsic anomaly of the kidneys in gouty subjects. The major abnormality appears to be "pre-renal", since the filtered urate load is apt to be excessive. The consequent increase in tubular reabsorption of filtered urate does not appear to exceed the normal response to increased filtered urate loads.

If the tubular reabsorption of urate is inhibited by uricosuric drugs, the urinary excretion of uric acid is enhanced and a state of negative urate balance supervenes. The beneficial results of such therapy in patients with tophaceous gout are described.

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THE PHYSIOLOGY OF HYPOTHERMIA*

JAMES E. ECKENHOFF

Professor of Anesthesiology, Schools of Medicine, University of Pennsylvania; Anesthetist, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

THE terms "hypothermia" and "artificial hibernation" are frequently confused. For clarification, hibernation in animals will be described first and then contrasted with hypothermia in man or animals. For a more definitive description of hibernation, one should read the excellent review by Lyman and Chetfield[1].

If one decreases the environmental temperature of a true hibernator such as a hamster, dormouse, hedgehog, ground squirrel or opossum, and makes the animal comfortable, the animal will curl up in a ball with nose beneath tail and tail around body and will go into hibernation. During this period the following observations can be made: Body temperature will decrease to about 4° C. or less; body metabolism will decrease to about 4 per cent of normal; respiratory rate may decrease to 1 or 2 per minute; the heart rate may fall from a starting level of 350 per minute to 5 to 20 per minute; the blood pressure declines to a low level, and no electrical activity can be detected in the cortex.

The animal will remain in this condition until he is either disturbed or until the environmental temperature begins to rise. Under these circumstances, the body temperature begins to rise and by the end of three hours has reached 38° C., the respiratory effort immediately begins to increase and over the period of several hours returns to its normal rate; the heart rate begins to rise rapidly, and if atrioventricular dissociation had previously been detectable, this disappears promptly; body metabolism and oxygen consumption increase rather abruptly, and continue to rise showing a definite over-shoot.

Under the above circumstances, a natural question arises as to the source of heat. One might assume that abdominal viscera, particularly the liver, might be the source, but this does not appear to be the answer,

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From the Department of Anesthesiology, Hospital of the University of Pennsylvania, and The Harrison Department of Surgical Research, University of Pennsylvania School of Medicine.

since eviscerated hamsters warm just about as fast as intact animals. The source of heat is more likely muscular activity. A completely curarized hamster will warm much more slowly than will a normal, untreated animal.

From the foregoing, certain obvious differences become apparent between a hibernating animal and a non-hibernating animal or man. The latter will not allow his own temperature to fall significantly without the external application of cold, nor having reached a body temperature of 25° to 27° C., will his temperature increase rapidly without the external application of heat. Certain other distinctions will become apparent with the development of the discussion. Obviously, the term "hibernation" cannot be applied to man.

In the application of hypothermia to man, the prime purpose is to reduce body metabolism and thus diminish the need for oxygen. A lowered body temperature can be obtained by the following means.

I. *External skin surface cooling applied to the body as a whole.*

A. Ice water immersion. Usually the anesthetized individual is immersed in water at body temperature and ice is added to the water subsequently. This is an effective method leading to a rapid fall in temperature.

B. Ice bags or plastic bags containing cooled fluid.

C. Cooling blanket—cold water or antifreeze solution is circulated through coils in a rubberized blanket. Warming is accomplished in a comparable manner with the same unit.

D. Suspension of body in a deep freeze unit.

II. *Internal surface cooling.*

A. Cold saline solutions poured into open chest following thoracotomy.

B. Circulation of cold fluid through a distended balloon in the stomach.

C. Application of cold sponges or pouring cold solutions about the aorta.

D. Ice water enemata. .

III. *Cooling blood removed from and returned to the body.* This method can be utilized for cooling the entire body, or for differential cooling of a single organ such as the brain.

A. Blood allowed to flow from an artery, passed through coils immersed in cold fluid and returned to a vein (heart acting as a pump).

B. Blood drawn from artery and by means of a booster pump, forced through a cooling unit and back into venous circulation. This method can be used with or without a simple blood oxygenator.

C. Blood drawn from superior vena cava or other major vein, cooled in coils and returned to another vein, such as the femoral, by means of a pump.

D. Blood removed from a major vein, cooled and pumped into the arterial circulation just above the aortic valve.

IV. *Adjuncts to cooling.*

A. Anesthesia—used to prevent shivering which increases oxygen demand, and to decrease body metabolism.

B. Relaxant drugs—used primarily to prevent muscular activity and shivering.

C. Chlorpromazine—also used to prevent shivering and to promote vascular dilatation. The trend today is to minimize the importance of phenothiazine derivatives in hypothermia.

The Effects of Hypothermia in Man

It is important to realize that due to an extensive variety of control conditions, reported data are at great variance[1]. The situation is being brought under control, but for this reason, controversial data will generally be omitted.

One major source of confusion has been a lack of accurate knowledge of body temperature. Usually, rectal temperatures are recorded, but Severinghaus has pointed out that temperatures recorded in this region may vary several degrees centigrade from esophageal temperatures taken near the heart[1]. Our clinical experience confirms this.

I. *Metabolism.* There is a linear relationship between body temperature and oxygen consumption. As temperature falls, so also does oxygen uptake. At 25° C., oxygen consumption is decreased by about 50 per cent.

While oxygen uptake is uniformly reduced in most of the organs studied, the effect of this reduction upon organ function is variable. In the liver, detoxification of drugs may be prolonged far out of pro-

portion to diminution in oxygen consumption. Thus the half life of morphine is increased from 3.7 minutes at 37° C. to 94 minutes at 24° C.[1]

II. *Cardiovascular.* There is also a linear relationship between body temperature and pulse rate, with the latter slowing gradually as temperature falls. Rates of 40 per minute are common at 25° C.

While a linear relationship also exists between temperature and mean blood pressure, this is not so clear cut. In general, blood pressure diminishes as temperature declines. The hypotension is most manifest below 30° C.

Blood flow and oxygen delivery to organ systems appear usually to be adequate. Studies have shown that the oxygen supply to the myocardium is adequate during hypothermia.

The effect of hypothermia upon cardiac rhythm follows a definite pattern, but here again the effects may vary widely from patient to patient depending upon many factors such as local oxygen supply, hypercapnia, blood pH, and electrolyte imbalance. The usual effects observed in the electrocardiogram in the temperature range of 32° to 28° C. include: Decreased amplitude or absent P waves, increased QRS interval, increased length of ST segment, and prolongation and/or inversion of T waves. If the temperature falls below 28° C. varying degrees of heart block may be manifest and ventricular extrasystoles and nodal rhythms may appear. As warming occurs, these changes disappear in reverse order.

Ventricular fibrillation, once so feared during hypothermia, is no longer thought to be a great problem provided the heart itself is not manipulated or operated upon. So long as correct electrolyte balance is maintained, as well as adequate oxygenation and pulmonary ventilation, ventricular fibrillation should be uncommon rather than common. If the heart is operated upon, other factors such as interference with local blood supply will increase the incidence of this complication. Two recent suggestions concerning the etiology of ventricular fibrillation during hypothermia are: 1) Development of a differential in temperature of various parts of the myocardium. The right ventricular wall temperature falls more rapidly than does the left, due to cold blood returning directly to that side[2]. 2) The increased susceptibility of the heart to adventitious stimuli during hypothermia and the development

of more rapid impulse transmission due to increased synaptic transmission[3]. Should ventricular fibrillation occur, it is hard to treat satisfactorily.

III. *Respiration.* The effects of hypothermia upon respiration are difficult to determine because of the confusion precipitated by use of preanesthetic drugs (e.g., narcotics and barbiturates) and anesthetics. It would appear that reasonably normal respiration can persist to well below 28° C. Hypothermia does increase the respiratory dead space[1]. Oxygen and carbon dioxide exchange do not appear to be affected. The oxygen dissociation curve is shifted to the left by hypothermia.

IV. *Central Nervous System.* One interesting difference between a hibernator and non-hibernator is that in the former nerves will conduct impulses almost to 0° C. whereas in the latter, conduction ceases below 10° C. In man, electrical cortical activity progressively diminishes as temperature falls until at about 18° C. electrical silence ensues.

It is difficult to predict at what temperature permanent damage to brain or nervous tissue may occur. Animals appear to be free of residual damage down to 20° C., but damage appears common below this. Several recent reports would suggest that temperature can be dropped far below this without damage occurring[1, 4].

Hypothermia offers several distinct advantages to the neurosurgeon. These include: 1) Marked decrease in cerebrospinal fluid pressure; 2) decrease in brain swelling at operation; 3) contraction of the brain, probably as a result of the decreased cerebrospinal fluid pressure; 4) decreased hemorrhage; and, 5) the brain is less vulnerable to operative trauma. However, there seems to be a decreased coagulability of blood probably due to diminished blood platelets. The latter disappear from the circulation at 20° C. The optimum temperature for neurosurgery is probably between 28° and 30° C.

V. *Renal Function.* Urinary output may be increased at 25° C. Reabsorption at the distal tubule is unchanged and excretion of water and sodium is unaltered.

A final question concerning hypothermia might be, "What is its present place in medicine?" Following the introduction and popularization of hypothermia, there was a fairly widespread use of the method in surgery. This use now appears to have diminished, primarily because

of the advent of successful extra-corporeal circulation for intracardiac operations. It will take some time before the true place of hypothermia is established.

Some of the uses for which hypothermia may be employed include: 1) Operations within the heart and upon the great vessels, e.g., aneurysms; 2) intracranial operations; 3) to reduce oxygen need in reversible conditions causing hypoxia such as in congenital heart disease, pulmonary, cerebral or peripheral embolus, and in anemic crises; 4) to combat hyperpyrexia as in thyrotoxicosis, brain lesions, heat stroke, and infections; and, 5) to reduce operative or anesthetic stress in poor-risk patients or those in shock.

The surgical uses of hypothermia have had extensive trial. Utilization of the technique for non-operative surgical or medical purposes is on the increase. We find today that one of our hypothermia units is almost constantly in use for non-operative conditions. The ultimate value of such therapy will require years to determine.

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AN OPERATIVE TECHNIQUE FOR ADRENALECTOMY*

JACK LAPIDES

Associate Professor of Surgery (Urology), University of Michigan; Chief, Section on Urology, Ann Arbor Veterans Administration Hospital; Acting Chief (Urology), Wayne County General Hospital, Detroit, Michigan

In recent years rapid strides have been made in delineating the normal physiology of the adrenal gland as well as the syndromes produced by its abnormal function. The advances in knowledge of the adrenals have effected an increase in the indications for adrenalectomy. In addition to Cushing's syndrome, adrenogenital syndrome, pheochromocytoma and adrenal neoplasms, extirpation of the adrenals has been performed for essential hypertension, carcinoma of the prostate, carcinoma of the breast, Kimmelstiel-Wilson's disease, primary aldosteronism and some types of secondary aldosteronism such as hepatic cirrhosis[1,2] and idiopathic edema[3]. Many of the individuals with these diseases are extremely poor operative risks because of impaired kidney, liver and cardiovascular functions.

In order for a precarious patient to survive an adrenalectomy, great pains must be taken in preoperative preparation and postoperative care. The operative procedure should be brief, relatively bloodless and potentially free of complications. In this paper a technique which apparently fulfills these criteria, is described. The method, except for a recent slight modification, has been employed by the Urology Section at the University of Michigan Medical Center for a number of years with excellent results.

PROCEDURE

Anesthesia. No routine anesthetic is employed. The agent, or agents, used in anesthetizing the patient is selected by the anesthesiologist in accord with the particular profile of the individual. All patients, how-

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From the Section of Urology, Department of Surgery, University of Michigan Medical Center, Ann Arbor, Michigan.

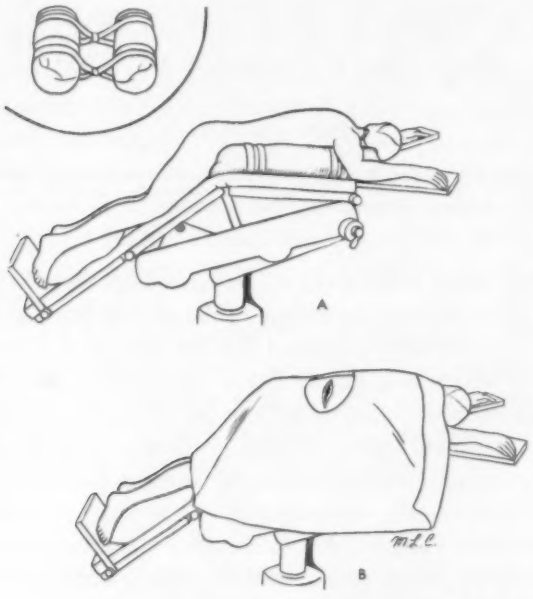

Figure 1. Position of patient on operating table during adrenalectomy. (A) Adequate pulmonary ventilation obtained by placing rolls along lateral aspect of thorax from shoulders to pelvis. Inset illustrates method of preventing displacement of supports during operation by lashing them together with figure of eight gauze strips. (B) After flexing the body by angulating the table, the thorax is made parallel with the floor.

ever, are intubated since the pleura is adjacent to the operative site and the pleural cavity may be entered during the procedure.

Posture of the Patient. After endotracheal intubation the patient is turned from the supine to the prone or face-down position. Adequate pulmonary ventilation is obtained by placing the individual on two rolls as illustrated in Figures 1A and 1B. Improvised supports can be made by rolling a pillow along its longitudinal axis and taping it circumferentially. The rolls are placed under the shoulders and along the lateral aspects of the thorax down to the pelvis. Displacement of the rolls during operation is prevented by lashing them together with several figure of eight gauze strips (inset, Figure 1).

After the patient is turned to the prone position and the symphysis aligned with the break in the table, the table is angulated so as to flex the

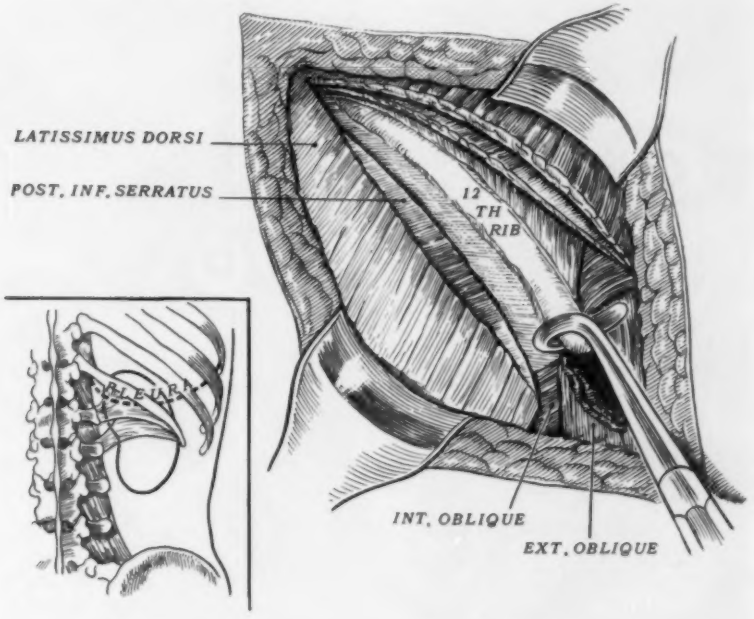

Figure 2. Surgical approach to the right adrenal gland. The Doyen rib elevator is being placed between the periosteum and bone at the very tip of the right 12th rib. Inset indicates position of the pleura in respect to the 12th rib.

patient's body. This maneuver serves to widen the intercostal spaces and increase the distance between the inferior costal margin and the iliac crest. The whole table is then adjusted to place the patient's back and thorax parallel with the floor.

Operative Technique: 1) Surgical approach: The adrenals are approached retroperitoneally through the region of the twelfth ribs. Two surgical teams of two members each make a simultaneous bilateral approach. In the group of four it is necessary to have only one experienced surgeon, a resident capable of removing a rib and two interns or medical students.

The skin incision is made over the twelfth rib extending medially from the outer border of the sacrospinalis muscles to several centimeters beyond the tip of the twelfth rib. The incision is carried rapidly down through subcutaneous tissue, latissimus dorsi, and posterior inferior ser-

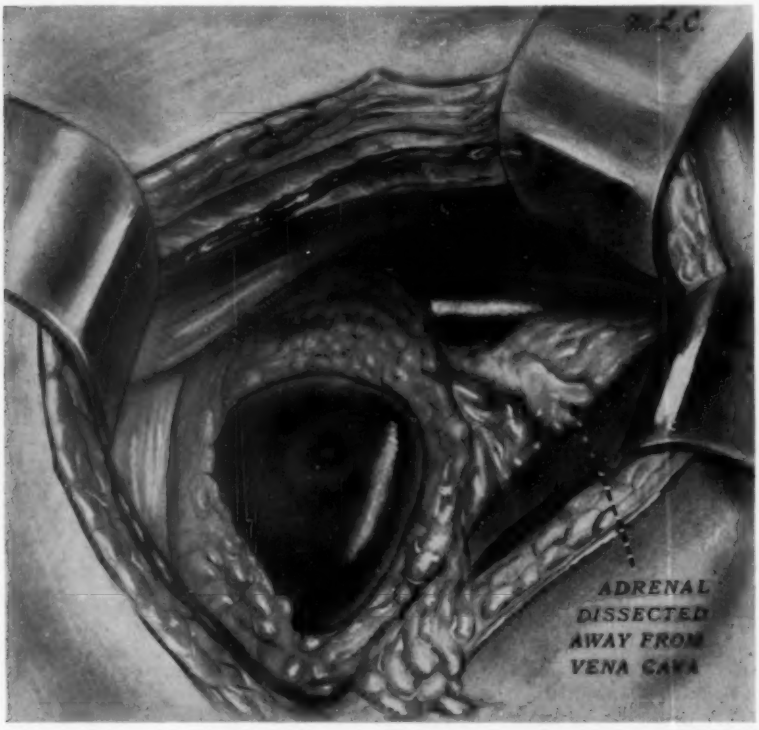

Figure 3. Relationship of the right adrenal gland to surrounding structures. Note that the adrenal is not in close relationship to the upper pole of the right kidney. A portion of the medial aspect of the adrenal overlies the inferior vena cava.

ratus muscles. The periosteum is incised along the midline of the rib and the attached muscles and periosteum are dissected free from the posterior surface of the rib with the Haight periosteal elevator. The anterior surface of the rib is separated from the periosteum with the use of the Doyen rib elevator which should be inserted initially under the tip of the rib anteriorly in order to avoid tearing the pleura (Figure 2). The pleura dips below the twelfth rib in the region of the costovertebral angle and may be perforated readily if one is slightly careless in placing the elevator under the rib near the vertebral column.

The rib is transected medial to the outer margin of the sacrospinalis and removed from the body after dissecting free the very tip of the rib.

In the process of cutting the tip of the twelfth rib free from its muscle and fascial attachments, a small opening is usually made through the lumbodorsal fascia into the retroperitoneal space. The small opening is enlarged to the margin of the sacrospinalis muscle by inserting the thumbs or index fingers and bluntly separating the lumbodorsal fascia posteriorly. By using the blunt method for enlarging the wound, injury to the peritoneum and pleura is avoided.

On entering the retroperitoneal space the posterior surface of the kidney with accompanying perinephric fascia and fat is observed.

2. *Exposure of the Adrenals:* The left adrenal gland is usually held in proximity to the superomedial surface of the left kidney by the perinephric fascia. Thus to expose the left adrenal, the left kidney is retracted downward and the fat lying superior and medial to the kidney is carefully cleaned away with long Russian tissue forceps until the yellowish orange color of the adrenal becomes apparent. The entire posterior surface of the adrenal is exposed as well as its peripheral outline.

In many instances the position of the right adrenal gland is not in accord with existing anatomical descriptions. Unlike the left adrenal the right adrenal gland may not be associated closely with the superomedial surface of the right kidney. Often the right adrenal gland lies higher than the upper pole of the kidney and its medial aspect partially covers the posterior surface of the inferior vena cava (Figure 3). It is also quite fixed in this position so that frequently it does not move down when the right kidney is pushed inferiorly. Occasionally the right adrenal will be adherent to the surface of the liver. Exposure of the right adrenal is accomplished in the same manner as described for the left gland. The important point to remember is that the right adrenal is usually much higher than the upper margin of the corresponding kidney and overlies the vena cava.

3. *Adrenalectomy:* Arterial vessels supplying the adrenal gland consist of a superior branch from the inferior phrenic, a middle branch from the aorta and an inferior branch from the renal artery; these arteries break up into a dozen or more fine branches before reaching the organ. Thus there are no large arteries entering the parenchyma of the gland[4]. The venous plexus of the left adrenal gland empties into a large vein which communicates with the left renal vein; the venous blood from the right suprarenal gland passes into a vein which drains directly

Figure 4. Technique of manipulative removal of adrenal gland. Note that the organ is held in the palm of the hand while the thumb and index finger are used to extract the vessel from the parenchyma.

into the inferior vena cava. Occasionally there are variations in the venous drainage of the right adrenal[5].

Until recently our technique in removing the adrenal gland involved ligating the vessels with either thread or metal clips. At the present time the author removes the adrenal by simply manipulating the vessels free from the organ (after the gland has been exposed and the surrounding fat dissected away). Figure 4 demonstrates the technique. Note that the gland is held in the palm of the hand while the index finger and thumb are used in extracting the vessels from the parenchyma of the gland. Never pull the gland away from its vessels for this may result in a tear

in the vena cava. The maneuver is usually accomplished in several minutes after which a pack is placed in the wound for four minutes. During the period of packing the surgeon can step over to the other side and remove the opposite adrenal in the same fashion. On removing the packs the wounds will usually be found to be dry. Penrose drains are inserted into the suprarenal areas and the wounds closed in an appropriate fashion. The drains are usually left in situ for a period of seven days in order to avoid abscesses in patients prone to infection.

Discussion

Fifteen patients have been subjected to adrenalectomy by the manipulative technique for such conditions as Cushing's syndrome, pheochromocytoma, primary aldosteronism, secondary aldosteronism, hypertension, mammary neoplasm and Kimmelstiel-Wilson's disease. Average operating time was one hour. Operative and immediate postoperative mortality was zero. The youngest patient was an infant three and one-half months old with primary aldosteronism[6]. In only one patient, our most recent, was it necessary to ligate the adrenal veins because of persistent hemorrhage; this individual with massive ascites had secondary aldosteronism associated with cirrhosis of the liver. It should be noted that the manipulative technique would not be used if abnormally large veins were encountered.

Although retroperitoneal pneumography has been made safe with the use of carbon dioxide as the gaseous medium, we have found this diagnostic procedure to be of little value in localizing most tumors of the adrenal. In the majority of cases it is necessary to expose both adrenals surgically and examine them. The simultaneous bilateral retroperitoneal approach permits exploration in a rapid safe manner—much safer than pneumography with gases other than CO_2. Postoperative paralytic ileus is minimized since manipulation of the intestines is avoided by staying out of the peritoneal cavity. Thus the care of the patient is simplified because oral food and fluids can be started within 24-48 hours after operation.

The most common objection to the employment of the retroperitoneal approach is usually voiced in relation to aberrant pheochromocytoma. The advocates of the transperitoneal route state that they can explore both adrenal areas and the bifurcation of the aorta without changing the patient's position and making another incision. Actually it

is quite simple when using the retroperitoneal approach, to extend one of the incisions anteriorly in the form of a hockeystick and explore the entire retroperitoneal area. Of course, it will be necessary first to close the patient's incision over the opposite rib and turn him to the lateral decubitus position; but this requires little time and effort.

Summary

A rapid, safe technique for unilateral or bilateral adrenalectomy is described. The technique employs a simultaneous bilateral retroperitoneal approach and a manipulative procedure for removing the adrenal glands.

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Transcript of

REPORT ON CONFERENCE ON PERINATAL MORTALITY

HELD AT THE NEW YORK ACADEMY OF MEDICINE

OCTOBER 29, 1957

FOREWORD

ON October 29, 1957 a Conference on Perinatal Mortality was held at The New York Academy of Medicine. The participants consisted of leading obstetricians, pediatricians, obstetric nurses, medical and nursing educators, hospital administrators, pathologists, anesthesiologists and representatives of other disciplines linked to maternal and infant health. There were also lay citizens, members of the public to whom maternal and infant care are directed.

The Conference grew out of the *Report on Perinatal Mortality in New York City* published by The New York Academy of Medicine two years previously. It was sponsored by the Academy, the New York Obstetrical Society, District No. II of the American Academy of Pediatrics, the Departments of Health and Hospitals of the City of New York, The Association for the Aid of Crippled Children, Maternity Center Association, Citizens' Committee for Children of New York City and the Community Council of Greater New York.

An interesting feature of the Conference was the atmosphere in which it was conceived and held. It grew, not out of any external pressures upon the participating agencies and disciplines, but out of a willingness and desire for self-examination and improvement. There was a general realization that something more and something different must be done if perinatal morbidity and mortality are to be lessened. With this was a recognition of the need to sit down and look objectively and critically at what is now done—or left undone.

Ten problems pinpointed in the *Report* were selected for discussion. The Conference was set up in ten tables of ten each; and one topic

was assigned to each table. Each table had a multidisciplinary constitution, with a discussion leader from the field most concerned with the question assigned. After a two-hour discussion period, the leader at each table reported the consensus of his group to the Conference as a whole.

The results of this informal and somewhat unorthodox procedure were most impressive. In addition to suggestions for long-term research, there were many practical proposals for improvements that can be instituted everywhere—now.

In the belief that the material in this report on the Conference speaks for itself, there is no editorial comment. Presented are simply a digest of the original *Report on Perinatal Mortality in New York City*, a copy of the ten questions asked, a list of the discussors, the consensus reported by each discussion leader, and the introduction and summary made by Dr. Leona Baumgartner, Commissioner of Health of New York City.

While the *Report on Perinatal Mortality*, which gave rise to the Conference, dealt with New York City only, much if not most of the material in it is applicable elsewhere. Certainly professional groups in other large urban areas will find a great deal that is recognizable and pertinent to their own communities. This report is published in the hope that it may stimulate discussions elsewhere which will produce additional helpful suggestions for the guidance of all.

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Association for the Aid of Crippled Children

Citizens' Committee for Children of New York City

Community Council of Greater New York

Department of Health, City of New York

Department of Hospitals, City of New York

Maternity Center Association

The New York Academy of Medicine

The New York Obstetrical Society

Participants in the Conference on Perinatal Mortality Held at The New York Academy of Medicine on October 29, 1957

PRESIDING

DR. LEONA BAUMGARTNER
Commissioner, Department of Health, City of New York

MR. LEONARD W. MAYO
Executive Director, Association for the Aid of Crippled Children

DR. HAROLD ABRAMSON, *Attending Pediatrician, Flower and Fifth Avenue Hospitals*

MRS. EDITH ALT, *Director of Community Resources, Health Insurance Plan*

DR. DOROTHY H. ANDERSEN, *Associate Attending Pathologist, Department of Pediatrics, Babies Hospital, Columbia-Presbyterian Medical Center*

DR. VIRGINIA APGAR, *Attending Anesthesiologist, Presbyterian Hospital*

MRS. MAX ASCOLI, *Chairman, Health Section, Citizens' Committee for Children of New York City*

DR. HARRY BAKWIN, *Professor of Clinical Pediatrics, New York University College of Medicine*

DR. HENRY L. BARNETT, *Professor and Chairman, Department of Pediatrics, Albert Einstein College of Medicine*

DR. CHARLES H. BAUER, *Chief Resident in Pediatrics, New York Hospital*

MR. DONALD B. BERG, *Research Assistant, Committee on Maternal and Child Care, Council on Medical Services, American Medical Association*

MISS BETTY BERNSTEIN, *Assistant to the Director, Citizens' Committee for Children of New York City*

DR. GILDDEN BROOKS, *Director, Health Research Institute, Brown University, Providence, R. I.*

DR. J. CLARENCE CHAMBERS, JR., *General Medical Superintendent, Department of Hospitals, City of New York*

DR. DUNCAN W. CLARK, *Professor of Environmental Medicine and Community Health, State University of New York, Downstate Medical Center, Brooklyn*

DR. VINCENT J. COLLINS, *Director of Anesthesiology, St. Vincent's Hospital*

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DR. JOSEPH V. CRESCI, *Attending Obstetrician and Gynecologist, Long Island College Hospital*

DR. HAROLD B. DAVIDSON, *Associate in Obstetrics and Gynecology, Lenox Hill Hospital*

DR. WILLIAM E. DAVIS, *Assistant Attending Obstetrician and Gynecologist, New York Hospital*

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DR. GORDON W. DOUGLAS, *Director, Department of Obstetrics and Gynecology, Bellevue Hospital*

DR. R. GORDON DOUGLAS, *Chief, Obstetrics and Gynecology, New York Hospital*

DR. MOREY R. FIELDS, *Director of Health Education, Department of Health, City of New York*

MRS. ALICE FITZGERALD, *Consultant, Association for the Aid of Crippled Children*

DR. JOSEPH A. GAINES, *Attending Gynecologist and Obstetrician, The Mount Sinai Hospital*

Dr. Harvey Gollance, *Medical Superintendent, Kings County Hospital*

Dr. Edwin M. Gold, *Associate Obstetrician and Gynecologist, Brooklyn Jewish Hospital*

Dr. Carl W. Goldmark, Jr., *Chairman, Special Committee on Infant Mortality, Medical Society of the County of New York*

Dr. Milton J. Goodfriend, *Director, Obstetrics and Gynecology, Morrisania Hospital*

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Dr. Henry B. Makover, *Professor of Preventive Medicine, Albert Einstein College of Medicine*

Miss Miriam Mangen, R.N., *Maternal and Newborn Division, Department of Health, City of New York*

Dr. Benjamin E. Marbury, *Associate Attending Anesthesiologist, New York Hospital*

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DIGEST OF

*PERINATAL MORTALITY IN NEW YORK CITY**

General Data:

As a basis for this discussion, we are accepting the following figures on perinatal mortality taken from a study of 955 deaths reported by the Subcommittee on Neonatal Mortality, Committee on Public Health, The New York Academy of Medicine, in 1955.

It is recognized that the sampling used may not be strictly representative, due to time factors, the fact that all death certificates were not available, and other biostatistical considerations. Interpretation was frequently hampered by the lack of an authoritative diagnosis: the cause entered on the death certificate and the clinical cause agreed only 42 per cent of the time and the clinical and pathological causes about 70 per cent of the time.

Nevertheless, for purposes of ascertaining responsible factors and seeking means of applying corrective methods, the sampling may be considered sufficiently representative.

The number of perinatal deaths studied and the percentage of preventability are set forth on the attached Table (Table I).

The responsibility factors most frequently present were: unavoidable disaster, 55 per cent; errors in medical judgment, 31 per cent; unsatisfactory pediatric care, 27 per cent; errors in medical technique, 24 per cent; faulty prenatal care, 22 per cent. Less frequent responsibility factors were: unqualified medical attendants, intercurrent infection, and family fault. These total more than 100 per cent because more than one responsibility factor was present in a number of the deaths.

Areas of Medical Responsibility:

Areas of medical responsibility included errors in medical judgment (28 per cent in the premature; 34 per cent in the mature infants); errors in medical techniques (16 per cent in the premature and 32 per cent in the mature infants); unqualified medical attendants (5 per cent in the premature and 9 per cent in the mature infants); unsatisfactory pediatric care (21 per cent in the premature and 33 per cent in mature infants).

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* A Study of 955 Deaths by the Subcommittee on Neonatal Mortality, Committee on Public Health, The New York Academy of Medicine. Analyzed and reported by Schuyler G. Kohl, M.S., M.D., Dr. P.H. Copyrighted and published by the Commonwealth Fund, 1955.

TABLE I

Category	*Stillbirth No.*	*Preventability Per cent*	*Neonatal Deaths (up to 6 days) No.*	*Preventability Per cent*	*Neonatal Deaths (up to 30 days) No.*	*Preventability Per cent*
Premature 1000 to 2500 grams	110	23%	279	32%	88	52%
Mature 2500 grams plus	127	35%	204	53%	147	45%
Total	237	29%	483	41%	235	48%

House staffs had the highest preventability rate and obstetricians the lowest.

There was a high incidence of operative deliveries: 46 per cent in the premature and 52 per cent in the mature infants, as contrasted with a more or less standard figure of approximately 30 per cent for all births. In this connection, more than 40 per cent of the deaths associated with cesarean section were adjudged to be preventable. A high degree of preventability was also ascribed to the deaths associated with deliveries in which high and mid-forceps were employed.

The choice of anesthesia and analgesia was associated with preventability of death. The birth of 50.8 per cent of the premature infants was associated with analgesia, and 60.2 per cent of the mature infants. Fifty-four per cent of the mature infants who died had been delivered under inhalation anesthesia; 21 per cent under local or low conduction anesthesia. Nevertheless, the frequency of preventability of death did not appear to be influenced by the anesthetic agent administered: the difference in the frequency of preventability between no anesthesia and inhalation anesthesia appeared to be insignificant. This degree of preventability was 29 per cent for premature infants, but 42 per cent for mature infants.

Hospital Factors:

The place of birth was associated with the following percentages of preventability of death:

Municipal teaching hospitals, 39 per cent
Municipal non-teaching hospitals, 50 per cent
Voluntary teaching hospitals, 21 per cent
Voluntary non-teaching hospitals, 35 per cent
Proprietary hospitals, 31 per cent

In other words, the incidence of preventable perinatal deaths was lowest in the voluntary teaching hospitals and highest in the municipal non-teaching hospitals. The preventable mortality rate was consistently higher in ward service cases than in private cases.

Relation of Preventability to the Mother:

The mothers having premature infants who succumbed were somewhat older than those having mature infants who succumbed. The highest frequency of preventability was in the age group 15 to 19.

There was a higher percentage of preventability for nulliparas, regardless of the infant's maturity and the age of the mother. This was particularly marked for mothers over 30.

Threatened abortion was associated with a higher percentage of premature (11.1 per cent) than mature (6.1 per cent) deaths. There appeared to be a pattern of perinatal loss in the obstetric experience of the mothers who bore the infants in this study.

There was a higher incidence of toxemia in the mother among the infants studied than for the city in general, especially among the stillbirths. Toxemia was present in the mother in 17 per cent of the premature infants and 15 per cent of the mature, as compared to 9 per cent in one large municipal hospital. As compared to an estimated 29 per cent preventability of all deaths, it was estimated that 48 per cent of the deaths associated with toxemia were preventable. The preventability for the premature stillbirths associated with toxemia was four times that for the premature stillbirths not associated with toxemia.

In this series there was a 28 per cent incidence of abnormal presentations for the premature and 14 per cent for the mature infants, contrasted to a 7 to 9 per cent frequency of abnormal presentations in all births. A higher mortality was associated with abnormal presentations.

Family Responsibility:

While the element of family fault was present, it was relatively slight. Miscellaneous family omissions and commissions at home were responsible for 5 per cent of the deaths in premature infants and 4 per cent in mature. Of more significance was the family's part in the factor of inadequate prenatal care, which was responsible for 23 per cent of the deaths in the premature and 20 per cent in the mature.

Introduction

DR. LEONA BAUMGARTNER

Commissioner, Department of Health, City of New York

It seems to me, as we meet here today, there is some value in looking backward to see where we've made gains in New York City in the past, and how.

I believe I am right in saying there have been four major attempts to do something about reducing infant and maternal mortality in New York City, at least three of which have left their mark, not only in this city but in the nation at large and even outside of our own country.

The first one had to do with the then new and miraculous idea, back in 1908, that one could prevent infant deaths. Doctors, by and large, in those days had taken care of *sick* babies. The idea that there was something that might be done to prevent a death was quite revolutionary; that there was something that might be done to prevent an illness; that doctors might do things to keep a baby well.

Down in a section of the lower East Side, a few blocks were laid out as a demonstration area to see what would happen if doctors and nurses went into underprivileged homes and demonstrated simple ways of preventing infant diarrheas particularly, and other kinds of illnesses in infants. That led to the creation in the Department of Health of the first Bureau of Child Health in the world. Today we have Bureaus of Maternal and Child Health in almost all the major countries.

The second attempt was perhaps a little different. It was made when Dr. Haven Emerson was Commissioner of Health and Hospitals, about 1916. The situation in relation to maternal and infant deaths was not too good. Women didn't come for prenatal care; or they didn't come early enough; we have many of the same problems today. There was a large study made, and an organizational plan was formed for districting of hospitals and districting of services—a plan which I must admit isn't too well carried out even now.

The third attempt dates to the 1930's, when the Maternity Center Association, the Department of Health and the Academy of Medicine, following the first maternal mortality study made by the Federal Children's Bureau elsewhere, set out the well-known maternal mortality study made in New York City. You may remember that the report

on this, published in 1933, outlined the major causes of maternal death as hemorrhage, toxemia and infection. It had a very interesting section that came out and said flatfootedly that two-thirds of these deaths were preventable; and it predicted that they would be prevented. I've always thought it interesting that we've done better than that!

That was a study, you remember, based on actual deaths, and it led to a lot of activity. It led to better education in obstetrics in medical schools; it led to better professional education of doctors and nurses who had already been graduated. It led to standards of prenatal care first set up, I believe, by the Kings County Medical Society and widely copied. It led to maternal mortality study committees, which have been a device widely used in our country, whereby doctors have kept on gathering the facts. It pointed to the need for research to learn better ways of preventing hemorrhage, toxemia and infection.

For us today, perhaps the significant thing to remember is that this report not only pointed to the need for research, but it said there are some things we can be doing while we are getting the new answers to our problems. We all know what happened.

New research brought the antibiotics; the wider use of blood and blood substitutes helped hemorrhage. There was better obstetric care of the obstetric emergency.

These innovations resulted from research; but greater awareness of what the patient needed, and what the medical and nursing team could do for the patient, also helped to bring about the better than two-thirds reduction in maternal mortality which resulted.

In the late 1940's, we began to get another movement. At that time we began to focus on perinatal deaths. Again, the idea was conceived essentially in this building. I well remember Dr. Corwin calling me up and saying, "Would you come up to a meeting of the Public Health Committee of the Academy and tell us some of the things you think might be done about maternal and infant deaths?" A study of perinatal deaths, similar to the earlier one on maternal deaths, was suggested. (It was an exciting day—a member of the Committee, Dr. Mustard, was unexpectedly sworn in that same afternoon as Commissioner of Health!) That wise body of men serving on the Public Health Committee of the Academy of Medicine agreed it might be well to repeat a study of the perinatal deaths in this city.

Two volumes have come out as a result of that study; the first, a

review of what is happening in our hospitals, which said that many things which were generally accepted as good practice were not being used in some institutions; and the second, a report which actually analyzed a series of neonatal deaths, to find out what the causes of death were and what we could do about them.

We are at the stage now, as I see it, to say, "What is it we can do about these facts?" And it is at this point that I think the groups represented at this Conference should begin and tell us what they believe can be done.

Question I

WHAT CAN BE DONE TO IMPROVE THE MANAGEMENT OF ABNORMAL PRESENTATIONS AND OPERATIVE DELIVERIES?

In this series, birth trauma was found to be an appreciable and important cause of death. High mortality (and high preventability) rates were associated with abnormal presentations and operative deliveries, particularly when labor was managed by other than qualified obstetricians.

1. How can better criteria be formulated for operative deliveries, covering critical points such as indications, timing, anesthesia?

2. What are the situations requiring qualified obstetric management and/or supervision?

3. Whose responsibility is it to define and supervise standards of techniques and qualifications?

DR. R. GORDON DOUGLAS, *Discussion Leader*

DR. HENRY L. BARNETT
MR. JOHN CONNORTON
DR. HARVEY GOLLANCE
MISS HATTIE HEMSCHEMEYER
DR. HAROLD JOHNSON
DR. HARVEY B. MATTHEWS
MISS HARRIET I. PICKENS
DR. MARTIN L. STONE
DR. TOBIAS WATSON

CONSENSUS

We have just barely had sufficient time to discuss all phases of the question presented to us. In order to save time, I shall limit my remarks to our conclusions concerning the specific questions referred to us. I think I'm correct in stating that we are in general agreement with the following statements:

It is of great importance in suspected abnormal presentation to have early and qualified consultations. In this community, this is frequently required if cesarean section is carried out; but it may be much more important if that type of delivery is not elected.

The second point is, that suspected abnormal presentation can only be determined with certainty under unfavorable circumstances by the use of an x-ray film. This is preferably done in early labor.

In making this decision, we discussed at some length the current thoughts concerning radiation hazards. It was generally agreed that, where there is reasonable doubt as to the presentation after consultation, the potential radiation hazard in skilled hands was much to be preferred to the possible outcome where malpresentation was not recognized.

The next question had to do with the possibility of the prevention of abnormal presentations. It was generally agreed that external version in breech and transverse presentation should be attempted if the membranes are intact and if there is an adequate amount of amniotic fluid. There were some differences of opinion with respect to when this procedure should be done; namely, just prior to the onset of labor or two, four, six or eight weeks prior to the expected date of confinement. It was generally agreed that this procedure should be done without anesthesia.

It was agreed that cesarean section is indicated for transverse presentation that cannot be corrected by external version; also in breech presentation where there is some other complicating factor, such as uterine inertia, large baby, tumor or other element interfering with the normal physiologic forces in labor. Cesarean section is indicated in brow presentation that is not corrected spontaneously or is not easily corrected by manipulation (conversion).

We were unanimous in our opinion that version and extraction in single pregnancy with a living baby is not a justifiable procedure, except under very unusual conditions. This brought up the question of how residents were to be trained in the art and technique of this

procedure. It was agreed that there are certain indications, on occasion, during the birth of the second twin, when this practice is justifiable. It was stressed, *on indication*, rather than routinely. Training of residents must necessarily be limited to these indications. Instruction can be augmented by use of the manikin.

We concluded from our discussions that the high preventability rate attributed to the resident staff in this report may not be a true representation of fact.

With respect to the specific three questions that were asked us, we would state, with regard to question number one, that frequent staff conferences, statistical studies and education at the local level by pathological conferences, joint obstetric-pediatric seminars, et cetera, constitute a most valuable means of promoting a high quality of obstetric care. This can be complemented by participation in regional and national scientific meetings and knowledge of the current literature. This inevitably brings up the question of how our community is presently organized for maternal care, and there is certainly some evidence to indicate that it leaves a good deal to be desired.

The second question can be answered as follows: That qualified obstetric management and/or supervision should be required on (a) all abnormal presentations, (b) all operative deliveries, other than outlet forceps, and (c) all patients in this category with an unfavorable obstetric history and those patients with medical complications.

The third and last question: It is at present the responsibility of the chief of each service to define and establish standards for his institution and the qualifications of personnel contributing to obstetric care.

Question II

HOW CAN THE HOSPITAL MONTHLY STAFF CONFERENCE BE MADE A MORE POTENT FACTOR IN IMPROVING MATERNITY CARE AND PREVENTING PERINATAL DEATHS?

There is need for an evaluation of all births since appraisal of many of the factors contributory to perinatal death requires more knowledge of their effects in surviving children as well as infants who succumb.

What can be done to improve the quality of material presented at monthly staff conferences? Accurate case records with a separate record for the infant? Improved autopsies? A central autopsy bureau? Follow-up of all children in whose birth suspect factors were present? Comprehensive consideration of data by obstetricians, pediatricians, pathologists, anesthesiologists and nurses?

DR. DUNCAN W. CLARK, *Discussion Leader*

DR. DOROTHY H. ANDERSEN
DR. HARRY BAKWIN
DR. WILLIAM E. DAVIS
MRS. ALICE FITZGERALD
DR. FREDERIC E. GROSSMAN
MRS. NATALIE LINDERHOLM
MISS MARGARET LOSTY
DR. LEON MOTYLOFF
DR. PETER M. MURRAY

CONSENSUS

We began with a critique of hospital staff conferences. What are the common practices and approaches? To what extent is consideration given the problems associated with perinatal mortality?

It was the belief of those at our table that many hospitals do not have perinatal conferences as such, and in not a few, there is a lack of interest in the subject.

There is also the question of whether perinatal conferences are held at a frequency that will do a great deal of good. Many are held only quarterly, apparently in order to accumulate statistical data of an amount thought necessary to give a picture of the experience of the institution in a standard unit of time. It may be that it is not really practical to hold such conferences more frequently. On the other hand, it seems unwise to delay or even omit the presentation and discussion of specific clinical incidents involving perinatal mortality shortly after their occurrence in the expectation that they will be part of a distant statistical review.

One spokesman at our table mentioned that at his institution special conferences are held which draw upon current prenatal clientele; these include representation from the variety of professional staff involved. It seemed to us this was an ideal kind of arrangement.

Consideration was also given to the need for regular hospital appraisal of the cause of death and the presumed responsible factors in every instance. This should be carried on in a spirit not of blame but of the

need to learn: the idea of assigning blame in cases thought preventable, might keep some of the staff away.

We thought, too, there were lessons to be learned, for use in regular hospital practice and conference method, from the techniques employed in appraisal and study in the Academy *Report*.

On the matter of attendance at hospital staff conferences, it was thought preferable that this be mandatory as a general rule, not only for the persons directly concerned but also for representation of the variety of fields associated with the obstetric service.

There is need for a consensus, it seemed to us, within the community at large and actually within the nation, on the use of such terms as "perinatal mortality", which we know to have a variety of definitions. We need, too, a more precise definition of "preventability" if this is to become a popular term, and also a specification of criteria for the use of this term.

There was discussion but no consensus on the question of whether a range of hospitals might become associated in a common effort to accumulate data and share their experience in order to give a larger corporate picture of the experience within a part of the community. There were different feelings about the practicality of this; it was believed that to some degree this cooperative effort is actually going on. One particular benefit from the practice might be its aid and impetus to standardization of some of the elements that are needed as a common practice.

On the question of autopsies (I mention such matters because they are subsidiary to things drawn upon in the presentation of staff conferences) there is obviously much need for a common effort at a more complete record in having autopsies performed on infants who die. On the question of the competence of the person to perform autopsies, the suggestion was made that a peripatetic pathologist, one especially interested in this kind of study, might visit the smaller hospitals.

Then there was the specific question: "Should there be a central registry or even a central autopsy bureau for those dying in the perinatal period?" We did not understand entirely what was meant by a "central autopsy bureau". If meant in the sense that there should be a central registry, this seemed desirable if not easily practicable. If meant that there should be a central place where such autopsies are performed, this was not thought desirable.

The question was raised whether the hospitals themselves might use some of the techniques of appraisal followed in the study for identifying responsibility factors. One limitation to this was thought to be the lack of field staff and of data obtainable through this means. The only obvious recourse is an effort toward the accumulation of such data regularly and routinely on all births. At the very least, there should be staff discussion of some of these cases and an effort at evaluation with the end in view of better records and better appraisal.

We wish to ask a series of questions, since questions have been addressed to us. To what extent has this Academy report been reviewed, as such, at obstetric and pediatric conferences in the hospitals of this city? Has it affected or changed the practices at any of these institutions? If this has not taken place to any considerable extent, is there necessary, perhaps, another translation of the report, possibly in a more popular form, for some obstetricians and pediatricians? In a form intended for hospital conference review?

On the question of records we said all the usual things you might expect. We were all on the side of the angels with respect to promptness of recording, adequacy of data, need of a unit system, inclusion of social data, etc. We have no specific suggestions as to how one can improve the human failings in record keeping.

The question was asked, should there be an independent hospital record for the baby in the hospital. We disagreed on this. There was a poignant question as to how long a baby had to live to warrant a record. When does his record begin? In the prenatal period? No consensus was reached.

Mention was made of the comprehensive care programs that are developing in some teaching hospitals. The possibility exists that certain programs created as instruments for medical education might also be instrumental in advancing other kinds of practice, concerned with the training of house staff and attending staff as well.

The problem continues as to who is responsible in some institutions for the newborn. The working relations of obstetric and pediatric departments need be always in sight and always in prospect of improvement. The size and nature of the problem of perinatal mortality is obviously one of the most important rallying points around which these services may wish to commit themselves.

Question III

WHAT CAN BE DONE TO IMPROVE THE PREPARATION AND SUPERVISION OF HOUSE STAFF PHYSICIANS RESPONSIBLE FOR WOMEN IN LABOR?

The relatively high preventability rate of perinatal deaths associated with labor managed by house staff physicians would seem to indicate they are not receiving adequate preparation and supervision. This is unfair to both the pregnant woman and the young physician.

What can be done to improve the preparation of interns in antepartal, intrapartal and postpartal care? How can proper supervision be insured so that when a woman in labor is cared for by a house staff physician it is safe for her and her child and a sound professional experience for the attendant?

DR. GILBERT J. VOSBURGH, *Discussion Leader*

DR. VINCENT J. COLLINS
DR. ROBERT L. CRAIG
MR. JOSEPH DERMER
DR. GORDON W. DOUGLAS
DR. MILTON J. GOODFRIEND
DR. ALFRED G. LANGMANN
DR. ABRAHAM C. POSNER
DR. AURA E. SEVERINGHAUS
MISS ERNESTINE WIEDENBACH

CONSENSUS

It should be said at the outset of this report that our group considered primarily the following sub-heading to our question: "The relatively high preventability of perinatal deaths associated with labor managed by house staff physicians, would seem to indicate they are not receiving adequate preparation and supervision. This is unfair both to the pregnant woman and the young physician." I will report our discussion in what I think is called a "stream of consciousness" style; we did not take time to organize the material in terms of specific recommendations.

The first answer to the question was an unqualified and emphatic single word, "money". Having disposed of the entire question and problem so very easily, we moved on to more esoteric considerations.

It was pointed out that frequently the people who are responsible for the care of the pregnant patient are working at cross purposes. The nurses are interested in one aspect of the patient's care; the house staff is interested in another aspect; the attending staff in a third aspect; and

the medical students, if there are such associated with the hospital in question, in perhaps still another aspect.

One of the major difficulties seems to be that the house officer is interested primarily in his own, I would like to say education, but I do not think the word is correct. He is primarily concerned with the acquisition of techniques and manual skills. He is interested in how to do forceps deliveries, how to do cesarean sections, and how to do breech extractions. In short, he is principally concerned with acquiring the manual dexterity which marks an obstetrician.

It was pointed out that the ability to use forceps was what differentiated an obstetrician from other surgical specialists. This becomes, then, a much sought after badge of distinction which can be worn only after reaching certain standards of proficiency in techniques. The house staff, it seems, is interested primarily in its own training and, perhaps too frequently, only secondarily in the care of the patient.

Much of our discussion revolved about the problem of house staff supervision. It was pointed out that in the voluntary teaching hospitals, which had the lowest perinatal mortality rate, there were many well qualified obstetricians immediately available; whereas in the non-teaching municipal hospitals the supervisor was frequently unavailable, at least from the standpoint of immediate supervision. In one instance which was described, there was a lapse of twelve hours before an attending supervisor could be located, reached, and brought to the hospital to help with the care and management of a patient with placenta abruptio.

That the question is not that simple, however, was pointed up by the observation that in some voluntary hospitals the immediate supervision is not so rigorous as in many other hospitals which had higher perinatal mortality rates. It seemed to our group that an area for further discussion could be found in the question, "Is immediate supervision necessary, or should the immediate supervision be primarily of a consultative nature with emphasis on long-range supervision in the form of education?" This point was developed with the observation that the supervisor who was asked to see an acute obstetric emergency—for example, a patient in difficulty on the delivery table—walked into a situation with which he was not at all well acquainted. He saw only the immediate problem and was not sufficiently familiar with other details which might bear on the advice he gave.

In such a situation, too frequently the solution proposed was incorrect. Even worse, there was no opportunity for further discussion be-

tween the house officer and his supervisor; and the opportunity to learn was lost. The desired continuity could be provided if there were a full-time staff; but this would be possible only if sufficient funds were available for the maintenance of such a senior staff.

It was pointed out that errors in judgment—for example, ill-advised operative interference or underestimation of the degree of hazard to mother and infant of an obstetric complication—accounted for most of the preventable perinatal losses. These could be circumvented by proper supervision provided the supervision was combined—before, during, and after the fact—with education.

The teaching of the house officer was discussed at some length. Several points were made. It is advisable to hold combined pediatric-obstetric-anesthesiologic conferences. The use of a scoring system of the condition of the newborn infant, such as introduced by Dr. Virginia Apgar, and insistence on the highest quality of medical records are useful not only in pinpointing problem areas when the work of the obstetric service is reviewed, but also as a teaching method.

One member of the panel proposed the introduction of a house officer school with a planned and prescribed curriculum which would emphasize fundamentals, broaden horizons and place in proper proportion the acquisition of manual skills. It was pointed out that frequently the quality of teaching is not commensurate with the problem at hand. The encouragement of research would lead to improvement in perinatal death rates, not solely by the advancement of knowledge, but also by the introduction of a better point of view that is an essential part of the scientific method. Again, the importance of informal discussion and consultation between members of the house staff and highly qualified senior people was emphasized.

Finally our attention turned to matters which were less concrete and more speculative. We asked but did not answer the question, "Is there an unavoidable inherent perinatal loss associated with the training of house officers?" We wondered whether the lessons learned by the military with respect to the triage of casualties should not be applied to the care of obstetric patients. Such a system would insist that the patient be seen first by the most experienced person; based on his evaluation, the problem and situation would be managed by persons of lesser experience. Our panel concluded with the observation that we needed to understand and make better use of motivation if we are to provide better care for the obstetric patient.

Question IV

HOW CAN ACTIVE MEASURES TO PREVENT PREMATURITY BE FOSTERED?

(In the study, a premature infant was defined as one weighing more than 1000 grams but less than 2500 grams)

The need for further research in environmental pathology, endometrial insufficiency, uterine anomalies and other possible organic factors in prematurity, while unfilled, is generally accepted. Although there is evidence that poor nutrition and other outgrowths of socio-economic inadequacy also contribute to prematurity, their role is less widely recognized.

Understanding of the total causation of prematurity would be furthered by socio-economic as well as medical research. How can comprehensive research in both areas be promoted and the findings correlated? How can physicians, hospitals and other community agencies, working together, implement the recommendations growing out of such research?

DR. S. Z. LEVINE, *Discussion Leader*

MRS. EDITH ALT
DR. CARL W. GOLDMARK, JR.
DR. PETER GRUENWALD
DR. ALAN F. GUTTMACHER
DR. NORMAN JOLLIFFE
DR. BENJAMIN E. MARBURY
DR. JEAN PAKTER
DR. BELA SCHICK
MRS. MARGARET STEWART

CONSENSUS

If prematurity could be prevented, perinatal mortality would be substantially reduced.

In New York City last year, 8.5 per cent of total births were premature. These accounted for two-thirds of the total perinatal mortality —for one-half of the fetal deaths and three-quarters of the postnatal deaths. It has been impossible, even under the most ideal conditions, to reduce premature mortality much below 20 per cent.

It costs the city $360 for hospitalization of the premature baby as against $100 for the full-term. Added to this initially higher cost for hospitalization, are further increased outlays for later institutional care,

since five times as many premature survivors require prolonged institutional care at a later date as do full-term survivors (3.5 vs. 0.7 per cent).

The high mortality (prematurity ranks eighth as a cause of death throughout the life span), the high morbidity, and the high cost of care all emphasize the importance of our subject—the prevention of prematurity.

The specific questions before us are: 1) What new lines of research might be undertaken to prolong gestation? and 2) How may current knowledge be applied more effectively? These approaches fall into three main areas: (a) maternal health; (b) local intra-uterine conditions; and (c) fetal factors.

The direct answer to the question of how to prevent prematurity requires new basic and applied research in these areas.

1. Strengthening of prenatal care: Even though facilities are available for better care, they are not utilized because of lack of public education, because of overcrowding and because of seeming disinterest on the part of the hospitals themselves.

2. There should be more prolonged antenatal hospitalization or enforced rest in multiple pregnancies. Posture plays a big role in precipitating premature delivery in multiple pregnancies; also in placenta previa.

3. Women who have small heart volumes and low hemoglobins during pregnancy should not engage in active physical labor; rest in these reduces the incidence of prematurity. Fatigue should be avoided in pregnancy.

4. Better nutrition. We are not sure of its specific role, but there is evidence suggestive of a relationship and we need research.

5. More social service case work.

6. Avoidance of meddlesome obstetrics and ill-advised induction of labor.

7. The establishment of coordinating committees of research with specific fields of study in habitual abortions; endocrine studies; physiology of the uterus with specific emphasis on induction of labor and initiation of uterine contractions; structure and physiology of placenta; role of nutrition in prematurity.

8. Improvement of laboratory services, including facilities for pertinent determinations in biochemistry, microbiology and immunology. Such services should keep abreast of latest developments in these fields; for example, staphylococcus typing, including phage typing, when possible.

Question V

HOW CAN A COMMON STANDARD BE ESTABLISHED FOR PERINATAL MORTALITY STUDIES?

Current studies of perinatal mortality vary in methods and nomenclature. This makes it difficult to correlate findings.

How can the disparity which often exists between clinical and pathological cause of death and the cause given on death certificates be eliminated? What can be done to foster more refined diagnosis and eliminate the use of such imprecise terms as "prematurity" as a cause of death? How can the quality of records be improved? A separate record for the infant, to make data more accessible for study? How can the results of different studies be made available more quickly to the various disciplines concerned with the problem?

DR. GEORGE M. WHEATLEY, *Discussion Leader*

MRS. MAX ASCOLI
MR. DONALD B. BERG
DR. EDWIN M. GOLD
DR. J. PHILIP LOMBARD
MR. SAM SHAPIRO
DR. LOTTE STRAUSS
MR. LOU WEINER
MISS DOROTHY WIEHL

CONSENSUS

One thing that the reports have not mentioned is the question of definition; namely, what are we talking about when we speak of "perinatal mortality". We thought clarification of this was necessary before we could discuss correlation of findings, one of the main questions aimed at us, and also before the magnitude of the problem could be measured. Much was said on this, as you can imagine, but we finally accepted a definition. It recognized that we are interested in the study of all babies, and would really like to measure all fetal deaths, but we also concluded that at the present time this is not practical.

In this connection there is one advantage that New York City has over a great many areas of the country; namely, the Sanitary Code of the city requires the reporting of all products of conception. This is an important point to bear in mind as we eventually improve our ability to measure the problem of perinatal mortality. In fact, this very Code, which is administered by the Health Department, was the basis for the World Health Organization definition of fetal death.

We agreed that we are concerned with the loss of life of an infant just before, during, or immediately after birth. The end points gave us some trouble. The period immediately after, we concluded, was seven days, though we realized that by adopting this cutoff point the opportunity to study some important aspects of the perinatal problem may be lost. Fixing the limits of the period of gestation was more difficult. In principle, there was recognition that 20 weeks of gestation or 400 grams was the lower limit; but that 1,000 grams, or 28 weeks, was the end point where practical life-saving work could at present be most productive. This must be kept in mind in dealing in a practical way with the problem we face today. We are trying to measure the loss in the area in which obstetric and pediatric care can be most effectively applied at the present time.

The perinatal mortality rate, it was brought out in our discussion, is useful for dramatizing the problem; but it may not adequately measure what pediatricians and obstetricians are accomplishing. It might be possible to evaluate this work more precisely if weight-specific death rates were developed. Progress would be easier to measure; and certain problems would actually be uncovered which are now masked by the perinatal mortality rate. At the present time the hospitals have these data but they need to be processed.

A previous speaker has recommended that an attempt be made to secure some accreditation for autopsies in fetal deaths in order to upgrade this activity in the minds of hospital administrators and medical boards. The American Academy of Pediatrics, at its last meeting, recommended to the Joint Commission on Accreditation of Hospitals that credit be given for such autopsies.

It is essential that efforts be continued to improve the hospital records and the reporting of accurate vital statistics. To motivate the house staff to take record keeping seriously, the head of the service must be impressed with the importance of keeping good records and provide leadership and direction to the staff. One factor that is helping to accomplish this, is the amended Sanitary Code of New York City, which now requires each maternity service and each newborn service to have a director. This puts the responsibility on the director of service for the maintenance of good records.

The development of comprehensive maternal and newborn records is something that should interest all hospitals. There are now 14 hospitals

in this city having records that can, so to speak, be interchanged. Ideally the 100 hospitals where there are obstetric services should have them.

The director of service should supervise the keeping of hospital records and see that they are kept up-to-date. One factor that might help implement this, would be the active interest in improved record keeping of the committees on maternal and child health of the county medical societies. Some of these committees are already engaged in this effort. The Joint Commission on Accreditation of Hospitals has been a motivating factor in raising the standards of record keeping in some of the smaller hospitals. We recommended perinatal conferences as a stimulant that would tend to improve record keeping.

A final recommendation would be the appointment of a coordinating committee of the five county medical societies to be concerned with perinatal problems.

Question VI

HOW CAN HOSPITALS, WITH OTHER AGENCIES, PROVIDE AN EXTENSION SERVICE AT HOME FOR MOTHERS AND INFANTS DELIVERED ON WARD SERVICES?

Mothers delivered on ward services are being discharged from the hospital three to seven days after delivery. When they return home, they may find themselves without a doctor and not know where to turn if the new baby does not thrive or becomes ill.

In the light of the growing emphasis on home care and continuity of care, might it not be feasible for hospitals to provide medical help by home visit, clinic facility or telephone consultation for mothers and babies delivered on their wards? How can such a service be set up? How can instruction in infant care be integrated with ward maternity service? How can adequate nutrition be assured for mother and baby once they are home?

DR. HENRY W. KOLBE, *Discussion Leader*

DR. CHARLES H. BAUER
DR. J. CLARENCE CHAMBERS, JR.
DR. NATHANIEL H. COOPER
MISS HELEN HALL
MISS MABEL V. JENSEN
DR. HARRY R. LITCHFIELD
DR. GEORGE W. MC CORMICK
DR. ROBERT S. MILLEN
MISS MARIAN RANDALL
MR. LEONARD A. TROPIN

CONSENSUS

Our first conclusion was that we would not solve the problem of perinatal deaths in New York City; but we proceeded from that point and have certain recommendations to submit. Most of these are not new; but we hope we can focus attention on some new aspects of the problem.

The subject that took up the major part of our discussion had to do with the extension of services into the home. It was our feeling and recommendation that hospitals should provide continuity of care by establishing an efficient system of telephonic communication after discharge. We refer, of course, to medically indigent patients.

There was considerable discussion of the roles of various agencies involved in this problem,—the Department of Health, the Visiting Nurse Association, the Department of Welfare, the Department of Hospitals, etc. One or two hospitals have established such a system, and it is apparently working successfully. We recommend that this practice be extended to all hospitals which operate obstetric services.

We cannot go into the details of how a system of telephonic communication with patients should be set up. That would be a problem to be solved at each institution, although certain basic principles should be kept in mind. I think those principles will emerge as I proceed with an account of the discussion held at our table.

In order to have proper continuity of service, we must recognize the fact that maternity care begins in the prenatal period with a proper program of education. We feel that education in the hospital is also essential, and should be emphasized to a far greater degree than it is at the present time. This educational program should be extended into the home by instruction previous to discharge of the patient and thereafter, as well as by suitable literature and instruction given at the time of discharge.

What was considered particularly important, especially in relation to our first recommendation, was that the mother and family be advised of symptoms and signs which would lead them to call the hospital for advice. With such a telephone system and educational program and the other facilities now available, we feel that this particular aspect of the problem can be taken care of satisfactorily.

We took cognizance of the fact that there is an emergency service at most hospitals; that there is an ambulance service; there are outpatient department facilities and public health facilities. All these were

taken into consideration in determining how the problem could be met.

The third problem we discussed was the matter of well-baby clinics. The Department of Health has a certain number of well-baby clinics; some hospitals also operate them. It is our recommendation that a study be made to determine whether there are adequate clinical facilities in this particular field to take care of the needs of the medically indigent population. If the survey should prove that additional clinics or expansion of existing clinics is indicated, it is of course our recommendation that this be done.

The fourth recommendation we have to offer is that voluntary health insurance plans be extended to care of the infant in the hospital and home, with exclusion of the ninety-day clause found in most plans.

The problem of how to be sure that mother and baby receive adequate nourishment after discharge from the hospital was also considered. Our recommendation was that adequate nourishment be made available for non-welfare clients who are eligible for welfare assistance, pending registration, by means of the social service department of the hospital, such funds to be dispensed through the Department of Welfare.

It was also recommended that information and data with regard to nutrition be included in the educational program, both in the prenatal and hospital period, and in the material given to the mother at the time of discharge from the hospital. In the same field it was recommended that selected cases presenting special nutritional problems be referred to the Visiting Nurse Service for follow-up; also that the Visiting Nurse Service check on nutrition of mother and infant at the time of each visit, regardless of the cause for that visit.

There was considerable discussion about the high perinatal mortality and morbidity associated with unmarried mothers. We had nothing special to recommend in this field except to emphasize that all the recommendations that we submit should be applied with special vigor to this particular group. It was, of course, recognized that the social problem is of paramount importance here. Unless it is resolved, proper service cannot be given to mother or infant.

Finally, we should like to point out that it is a policy of hospitals with ambulance services to bring mother and infant into the hospital when delivery occurs in the home. It is felt that the importance of this should be emphasized; and that physicians in attendance on such calls make very clear to mother and family the necessity of coming into the hospital for follow-up care.

Question VII

HOW CAN PRENATAL CARE BE IMPROVED?

Many expectant mothers who have heard of the importance of early registration for continuous maternity care nevertheless fail to seek care early or return for scheduled visits. They are dissatisfied with the conditions under which service is provided.

How can the pattern of prenatal care, in clinics and elsewhere, be made more pleasing to expectant parents and more effective medically? More comprehensive study of each woman? An appointment system so the mother need not wait for hours in order to be seen for only a few minutes? More practical help with nutrition and other factors in daily living which make for health? Continuity in the professional staff attending her? Time in which to establish a relationship with doctor, nurse or social worker so she will feel free to ask questions and talk out fears?

How can language and cultural difficulties be overcome and the pattern of care adapted to the needs and attitudes of different population groups?

DR. LOUIS M. HELLMAN, *Discussion Leader*

MISS HAZEL CORBIN	DR. RICHARD N. PIERSON
DR. ELEANOR HAMILTON	DR. HERBERT H. POMERANCE
MISS EDITH HARRIS	MISS EMILY STAMM
DR. ROSCOE P. KANDLE	MISS MARY WALLACE

DR. BERNARD A. G. WEISL

CONSENSUS

The problem of prenatal care in modern obstetrics seems to be one of simple logistics, particularly in municipal hospitals. In New York, as elsewhere, we are dealing with an explosive birth rate and an explosive increase in population. In Manhattan it is estimated that by 1965 one-half of all deliveries will be of medically indigent patients. The omission of prenatal care in this borough is rising about 2 per cent per year. This reflects the marked increase in the number of individuals who are seeking care and who are unable to find it in a satisfactory manner. It is suggested that this situation, and perhaps some of the patients' dissatisfaction, particularly with the postpartum aspects of their obstetric

care, might be somewhat alleviated if contraceptive advice were given to patients, especially in municipal hospitals where its dissemination is now prohibited.

The following suggestions are presented as an attempt to find a solution.

We are in strong agreement that one of the things that must be instituted in prenatal clinics is an appointment system. This would relieve the strain on the physician and the patient alike. It would both save time and enable the physician to give the patient better care. We realize full well that this is costly, for an appointment system requires the addition of personnel. It also requires an adequate medical staff to meet the patients once they are in the hospital. However, judging from the experience at Sloane Hospital, the number of missed appointments could probably be cut in half, and the time the patient spends in the clinic reduced by 50 per cent, by this one innovation.

We recommend increased attention to the organization of the out-patient department. If the amount of medical or administrative attention given to the out-patient prenatal clinic were equal to that now given to the delivery floor, the situation in the former could not help but be improved. Particularly we recommend that a director of the prenatal clinic, completely responsible for its operation, be appointed. Preferably this director would be a salaried physician.

We recommend an increase in the amount of education provided patients in the out-patient department and at the postpartum visit so they may feel the experience has been worth while. This need not be an elaborate program. It could be instituted with the use of already available motion pictures or other illustrative material and devices that the patients could look at while spending an interminable number of woman-hours waiting for their two or three-minute medical visit.

Finally, we think that the whole situation of out-patient care ought to be examined for a new approach, particularly in regard to personnel. In the light of the increasing population, and in view of what may be expected in the next ten years, we can foresee a serious shortage of qualified people to give prenatal care. There will be neither a sufficient number of physicians nor a sufficient number of nurses. We can no longer rely on voluntary physician help given by the community doctors. They do not now and will not in the future have enough time; nor will there be enough of them. Therefore, we suggest the use of paramedical personnel, and that particular attention be paid to the development and use of nurse-midwives within our obstetric hospitals.

Question VIII

HOW CAN THE PUBLIC BE HELPED TO UNDERSTAND THE IMPORTANCE OF EARLY REGISTRATION AND OTHER HEALTH MEASURES IN MATERNITY CARE?

Perinatal mortality is highest among expectant mothers applying for clinic and ward service. Many of them still register in the late months of pregnancy, leaving little opportunity for the application of measures that might reduce the rate of abortion, prematurity and stillbirths.

Whose responsibility is it to see that existing knowledge for the promotion of positive health is made available to expectant parents, and to help them apply such knowledge in their daily lives? Whose responsibility is it, for instance, to teach people proper practical nutrition? How can physicians and prenatal clinics help low-income patients to get the food they need?

How can language and cultural differences that make it difficult to communicate with some population groups be overcome?

DR. MOREY FIELDS, *Discussion Leader*

MISS BETTY BERNSTEIN	MISS MIRIAM MANGEN
DR. JOSEPH V. CRESCI	MRS. THEODOR OXHOLM
MR. HORACE H. HUGHES	MRS. RUTH SEIDLER
DR. JONATHAN T. LANMAN	DR. FANNIE TOMSON
DR. HENRY MAKOVER	MR. EARL UBELL

CONSENSUS

You will agree, of course, that this is one of the most important parts of this conference because, regardless of what information is received by a woman, the major responsibility for prevention or control of perinatal problems lies largely in her own hands. If she does not desire to seek early care and to act on recommendations, then the information has been valueless.

As a first problem we saw certain needs. One was more information about why people who desire the services do not come to take advantage of them. We talked about why people come and why they don't. We identified many reasons, such as hard clinic benches, sour faces and unpleasant experiences. But we also brought out that we have not been

finding out what motivates people to take action for early maternity care. We think that just giving people information will not cause them to behave the way they should behave; mere words do not bring action.

The second item we identified as a need was more information on perinatal causes of mortality. For a while we threatened to settle down in a discussion on the scientific bases for the information that could be used. But we eventually agreed that more information is needed.

The third need we identified was that of starting earlier to get information to people. When we tried to define "earlier" we went way back; we were not certain how far back we should go. We could not arrive at any specific age period; but we suspected that it was important to catch the female child much before she was in a position to become pregnant.

Then, the fourth need we identified was that of applying more effective methods of getting action by people. As we went deeper into our discussion we noted that we are not reaching the age group and the cultural and ethnic groups that need to be reached.

There was a second problem. We didn't know the accessibility or adequacy of services that were being offered, and how these affected the people who were trying to seek these services, or the people whom we wanted to use these services.

A third problem was that certain agencies were not taking responsibility for carrying out education in this area. We talked specifically about the schools, and said that the schools needed to do a job of education. However, many teachers are not adequately prepared in the understanding of perinatal problems.

A fourth problem involved a realization of the many different cultural patterns and attitudes concerning maternity problems, children, living together, and families, and that many obstacles to education had to be overcome before our process could be effective.

A fifth problem was concerned with the inaccessibility of available services, particularly to the clinic group. It is difficult to get people to go beyond their own door to attend a clinic service which is not readily accessible. We talked about a mobile, built-in clinic service that we could take along to the house; when we rang the doorbell, we could offer the service at that time.

Then, one problem which was raised, but about which we didn't come to any specific conclusion, was the possibility that patients using

clinic services stayed away from the clinics because they believed they were being "practiced on".

How to reach those groups of people who need the maternity care services, took up some additional time in our discussion. We thought that groups could be approached largely through the community agencies. The schools could reach a large number of girls who would probably drop out at a certain time in their school life, to get married shortly thereafter. Use of other agencies in the community would be necessary to reach the people, with the Health Department taking responsibility for programs geared to the needs of the community, and based specifically on what had been learned through research in motivation.

We did not have any idea of trying to control the thinking of those who should be reached with perinatal information. In some cases it was believed important to break through cultural barriers. We felt it would be very important to reach certain language and cultural groups through related language and cultural experiences, such as having persons on the staff who understood the backgrounds of the people, and who would be able to work within whatever ethnic and languag characteristics existed.

About responsibility, we said the Health Department had the primary burden, because it was a public health problem. The practicing physician, hospitals, schools, churches, family agencies and other community agencies could also make contributions to the solution of the problem of how the public could be helped to understand the need for early maternal care.

We next considered answers to the specific questions presented to our group. Whose responsibility is it to see that existing knowledge for the promotion of positive health is made available to expectant parents and to help them apply such knowledge in their daily lives? We had a very community-minded group. We said, "Everybody's; everybody who has some share and who has an interest or concern in the problem." We specifically indicated that the Health Department should take leadership.

And how can language and cultural differences, that make it difficult to communicate with some population groups, be overcome? We specified the need for persons who understand the cultural patterns and languages to work directly with each language or cultural group.

Then we concluded we had to develop better techniques for educating those who come to receive our perinatal services. Therefore, we felt it would be desirable to improve our educational process. That can only be achieved by learning more about the people with whom we are working. If we are going to reach people, we need to find the factors that will move people to action.

Question IX

WHAT IS THE RELATIONSHIP BETWEEN OBSTETRIC ANESTHESIA AND ANALGESIA AND PERINATAL MORBIDITY AND MORTALITY?

Many neurologic disorders, as well as perinatal deaths, are attributed to anoxia at various stages of intrauterine life and during labor. This suggests the need to restudy its relationship to intrapartal anesthesia and analgesia.

How can an accurate re-evaluation be made of the indications for the use of anesthesia and analgesia in labor and the effects of specific agents? What should be the qualifications of those giving obstetric anesthesia? How can adequate supervision be insured when anesthesia is given by other than a qualified anesthetist?

DR. VIRGINIA APGAR, *Discussion Leader*

DR. HAROLD ABRAMSON
DR. GLIDDEN BROOKS
DR. HAROLD DAVIDSON
DR. SOLOMON G. HERSHEY
DR. RICHARD L. MASLAND
MR. LEONARD W. MAYO
DR. VERONICA O'BRIEN
DR. CHARLES REINER
DR. SEYMOUR ROMNEY
DR. WILLIAM A. SILVERMAN

CONSENSUS

Those at our table were alternately anesthetized and resuscitated, and we all survived with no morbidity or mortality!

We agreed immediately on one thing: that there is no conclusive evidence to indicate a relationship between neurologic disorders and obstetric anesthesia and analgesia. We were a little bit unhappy about the wording of the first two sentences presented to us, which read as follows: "Many neurologic disorders as well as perinatal deaths are attributed to anoxia at various stages in uterine life and during labor. This suggests the need to restudy its relationship to intrapartal anesthesia and analgesia." Mr. Mayo labelled this "a value judgment". We do feel though, because of the various strong emotions surrounding the question of anesthesia and analgesia and neurologic disorders, and a theoretical possibility that this is one of many facets in such a relationship, that the question does indeed need to be investigated further.

From the clinical side there are three suggestions as to how to collect the data; as for interpretation, we'll just have to let that go because that, of course, is the hardest part; but first, the data.

Right now, under Dr. Masland's direction, a collaborative cerebral palsy study is under way, in at least 15 institutions. This will cover about 7500 babies a year, who will be followed practically from the moment of conception to about six years of development. This study will deal with many facets including anesthesia and analgesia.

As Dr. Kohl has already indicated, perinatal studies of obstetric services right here in this city will afford very valuable data. They should be on a prospective basis and not be retrospective.

Third, studies with random selection of anesthetic agents, very like the Johns Hopkins series, should be done in teaching institutions.

Another angle, of course, has to do with basic research. Basic research is needed to "confront conviction with data". That's from Dr. Brooks.

The factors surrounding birth—particularly human uterine physiology, the intrapartal changes, what happens to the baby as he passes through the bony pelvis to the outside world, immediate adjustments to extrauterine life—all need great attention. We stress the word "human" here; no more animals—hamsters, monkeys, sheep, etc. It's impossible to go from species to species, and we are dealing with the human species.

The problems of manometry, particularly that in the infant-size samples of blood for gasometry, etc., need amplification. There are unlimited fields for research in just the realm of manometry. As yet, there are hardly any data at all about these various aspects.

A part of the question has to do with the qualifications of the person giving obstetric anesthesia and with adequate supervision. How can the latter be assured if anesthesia is given by other than a qualified anesthetist? We believe that both of these problems can be solved if, in any hospital with an obstetric service, there is an organized anesthesia service. Of course, it's even better if the anesthesiologist has some interest in obstetrics and knows something about it; and that is often not the case. However, with an organized anesthesia service, the anesthesiologist can supervise the person who is to give anesthesia.

Someone in the hospital responsible for training and supervision would help solve this problem. I know there are difficulties in the way of this but that was the thought of those at our table. It is obvious that the competence of the anesthetist in handling individual circumstances is important, and whoever it may be should be under the direct supervision of the medical anesthesiologist.

We got nowhere trying to make recommendations as to what kind of anesthetic agents to use. There really are no data about this: a whole lot of ideas but nothing in the way of facts.

There seemed to be some suggestion and a little bit of agreement (I had to talk some people into this) that in many obstetric situations regional anesthesia procedures ought to be preferred to general anesthetic techniques. It is true that some obstetric complications requiring operative procedures, such as version with breech extraction and repair of a vaginal wall tear, require general anesthesia for relaxation; and there are situations that cannot be handled by pudendal block or local anesthesia. The stressing of regional techniques is probably more important in hospitals where there is no competent anesthesiologist; but if it is true there, I do not see why this should not also be true in hospitals that do have anesthesiologists.

Question X

WHAT CAN BE DONE TO LESSEN THE INCIDENCE OF PERINATAL DEATHS RESULTING FROM MATERNAL COMPLICATIONS?

There was a high incidence of toxemia and threatened abortion in this series of births. Expanded research into maternal complications, including study of socio-psycho-economic causes and follow-up of surviving infants whose births were associated with complications, would help to clarify the latter's role in perinatal deaths.

How can coordinated research by obstetricians, physiologists, pathologists, embryologists, geneticists, pediatricians, psychiatrists, nutritionists and sociologists be set in motion to increase our understanding of maternal complications and their role in reproductive failure?

DR. BERNARD J. PISANI, *Discussion Leader*

DR. GEORGE W. CORNER
DR. HOWARD R. CRAIG
DR. D. ANTHONY D'ESOPO
DR. JOSEPH A. GAINES
DR. HORACE L. HODES
DR. HAROLD JACOBZINER
DR. MILTON D. KLEIN
DR. HARRY D. KRUSE
MISS GRACE NAISMITH
MRS. HELEN OWENS
DR. RANDOLPH A. WYMAN

CONSENSUS

We reviewed some aspects of clinical and basic research in attacking the problem of perinatal mortality.

First, emphasis was placed upon the need of a multidisciplined approach under superior leadership, whether the research be clinical investigation or basic scientific study. On the research team will be the obstetrician, pediatrician, nutritionist, physiologist and sociologist. Add to these the anesthesiologist, embryologist and geneticist. Then, as brought out today, the necessity for mutual understanding regarding nomenclature and common terminology was stressed.

Correlation of the multiple studies on nutrition offers fertile fields for research. This study, based on diet alone, might fail because it is recognized that a "good diet" may not assure a state of good nutrition. So we seek aid from the physiologist, nutritionist and dietitian in as

simple an example as this one. The clinician contributes too, because in chronic disease, when nutritional states are frequently poor, the patient's reserve is lowered; and it takes little to put her into an acute phase of disease in which catastrophe may result. This certainly is a problem for both basic and clinical research.

A few recommendations were made in the field of basic scientific studies. For example, there should be a consideration of embryological factors and the roles they play. If it were possible, as one of those at our table put it, to have a "womb with a view", the embryologists and the physiologists would be able to study every stage of gestation. Since direct observation is impossible, the members agreed that this is not a perinatal problem although it was felt that many studies of applied embryology could help to obtain normal infants.

This also brought forth consideration of some fields of genetics. Immediate recognition was given to the fact that man, as a rational animal in our present society, cannot be regimented by codes or regulations arising from purely genetic laws. Although there are important concepts and practical theories in this field of science, man is a free agent in many aspects of human reproductive behavior.

Another field of basic scientific research is found in those conditions associated with virus infections in early pregnancy. The safe, normal development of the embryonic plate from the sixth to the twelfth week of intrauterine life is probably the greatest and most important biological factor in the life blood of this nation. Therefore, scientific care and attention to the health of the pregnant woman during this period cannot be given too much emphasis.

There are many areas of applied clinical research to consider. One suggestion presented today was more careful screening, by examination, of the pregnant woman, both in the clinic and in private practice. But would any hospital medical service in this city be willing or able to accept 2500 to 3000 new patients per year, examining each one routinely, but comprehensively and thoroughly, before turning her over to their obstetric colleagues?

Possibly such a pilot study does exist. If so, are the results important enough to warrant the added financial burden and clinical effort? There are further reflections concerning a project such as this. For example, is this type of screening necessary when, in our better hospitals and teaching institutions today, the medical student, intern, resident and

attending staffs of the obstetric services study all aspects of the physical condition of these patients as a well established routine? Would further study be feasible or rewarding?

With our city's changing population, language difficulty often requires the addition of an interpreter to the clinical research team. This results in an increase in the already considerable amount of time spent with the patient.

Another region worthy of investigation would involve a study of the home-care program and its effect on perinatal mortality in many chronically ill women who require special medical attention. In this same vein, we should study and evaluate our prenatal education and care routines, improving them where necessary.

Efforts at improvement in this area can be divided into three fields, —the clinic patient, the private patient, and the physician. For example, what are the best media for prenatal education of the service patient? The hospital and clinic are first. Can the press also help? What role could it play if it avoided the sensational and did not put emphasis on the bizarre? Is this true also of radio and television? Can much be done to help those who do not or cannot read? The physician plays a role in the education of the private patient and in so doing contributes to studies in applied clinical research.

The carefully planned perinatal mortality conference is one of the best ways to teach the doctor, from medical student to qualified obstetrician or pediatrician. In the free and open discussion that takes place in this type of meeting every cause of perinatal morbidity or mortality would be encountered. These conferences should be part of the regular program of the obstetric service in all hospitals.

At the county medical society level, committee study of infant deaths is equally valuable. In New York County the Committee on Infant Mortality has done a magnificent job and already has published three revealing reports, in addition to holding quarterly symposia for obstetricians, pediatricians and other members of the medical profession interested in this topic.

Studies by the Maternal Mortality Committees of the county medical societies also provide us with valuable information; an analysis of each maternal death is always accompanied by a report of the perinatal status of the infant. These conferences provide excellent material for clinical research for all physicians.

In promoting wider application of what is known about patient care, we will obtain better results in physiological research because individual problems will be more sharply defined.

It is also proposed by our discussion group that much could be done by circularizing physicians with new material on progress and on up-to-date management of the many phases of pregnancy and labor. This could take the form of carefully prepared messages similar in format to the small brochures distributed to practicing physicians by the American Cancer Society. Current reports on scientific progress in anesthesia, in the field of obstetric physiology, management of habitual abortion and the toxemias, would come under this heading and certainly would be a part of an educational program aligned with clinical research.

One further word about personnel. There is today, and there will probably continue to be for some time, a great dearth of qualified persons in research to cover adequately the many facets that have been reviewed here today. There are not enough interpreters. There are not enough social workers. All hospitals cannot have superior anesthesiologic coverage 24 hours a day. Enough capable nurse-midwives are not available to help the obstetrician.

This shortage in clinical research is similar to the well known personnel shortage in basic research. It is interesting to view the statement of Dr. Yankauer, New York State Department of Health. Speaking on this topic, he says, "There is need for basic research. What are the basic causes of placenta previa, of abruptio or toxemia or premature labor? What is the histochemical change or the mechanism that produces the condition labelled abnormal pulmonary ventilation? There are large groups of perinatal deaths with no obvious associated cause and it is unlikely that answers will come from either epidemiological inference or clinico-pathologic study as we knew them in the past. There is again need for basic research." In the report of Dr. Kohl and his committee, reviewed today, this fact has been brought out.

And now to close, with a single note on clinical research. The clinical obstetrician is responsible for the individual case. He has the obligation to preserve the life of the mother and the life of this new citizen we have been discussing. These are irrevocable trusts. He always welcomes the support and cooperation of his colleagues working in other disciplines. He realizes how very much he does need their help.

Would that all of these talents and knowledge were available at every early morning hour when the dangers reviewed may present themselves, when the obstetrician often finds himself without the services of the anesthetist or the pediatrician, or of anyone else.

Summary

DR. LEONA BAUMGARTNER
Commissioner, Department of Health, City of New York

Two things have highlighted this discussion. There has been, first of all, an overtone in every single report: every chairman has said in some way that what we need in this field is not more of the same, but something different. We need a new attitude, a new approach, new knowledge, maybe even a new philosophy.

Dr. Hellman told us why we need it desperately right now in New York City; and that is because of what he called our explosive birthrate. By 1965 half of our births will be in the medically indigent group, whereas for years we have estimated that only about 20 to 25 per cent of them would be in that group.

Secondly, it was said that this problem is not just the doctors' business, not just the pregnant woman's business, not just the visiting nurses' business; but everybody's business. We desperately need to bring the patient in on the team; and we need to do something for her even before she becomes a patient. These are some of the overtones that ought to lead to new philosophies and new programs of action.

As to specifics,—we need a great amount of research of all kinds. There are so many questions to which we don't have the answers.

Some of the problems require basic research; others, applied clinical research. Some are in the area of operational problems, such as determining whether there is adequate service for an apparently well baby; and if not, getting adequate service. Some of us tackled the problem of motivation, of why people don't use services. There was the suggestion that we did not know how to deal with the unmarried mother and that it is time we found out how to manage her problems.

But I think it of interest that several rather simple techniques were proposed. The idea was suggested several times that coordinating committees of research, tackling the various specific problems relating

to premature labor, anesthesia, etc., would be helpful. That is a technique that can be developed or expanded right now.

Another suggestion recommended the extension of a device that is already in existence in some hospitals; namely, the interchangeable record. If all of our hospitals had the same standard, combined maternal and infant record, we could more easily gather data that are comparable. These are easy research techniques, if we are willing to adopt a new attitude.

It is easy to sit back and say, "Let's wait until the new research comes along and then we'll know what to do." The 1933 mortality conference group did not wait for all the antibiotics to come along before doing something about infection; they did not wait for new knowledge; they started out by putting into practice what was already known. They did some things right away; and we too listed a fair number of things that we can start doing as of tomorrow morning.

About the staff conference, we said it came too little, and it came too late. It was suggested that the pathologists might be able to build more interest in, and contribute more of value, to the staff conference. For the small hospital that does not have a pathologist, a visiting one was proposed. All this could be started now, perhaps through a working committee of the five county medical societies. The Joint Commission on Accreditation of Hospitals could also help by giving credit for autopsies in perinatal deaths.

A lot was said about consultation; in essence, that wider and better use should be made of people who know more to help those who know less. A roster of those who could help would include the qualified attending medical staff, the nurse who knows more, the anesthesiologist, the nutritionist, the social worker, the psychiatrist, etc.

One very important thing was said in this connection. These people should not just be listed on the hospital letterhead; they should not just be mentioned in the annual report; and they should not just be known as the chief of service. All up and down the line they should be available, and immediately, all the time, 24 hours around the clock. It was hinted that this was probably the most important single reason why the teaching hospitals had the outstanding record they did in the study under discussion here.

This help and this consultation should not be a matter of lip service to an idea. It should be required and it is up to the directors of the

obstetric and the pediatric services to see that it is carried out. In the obstetric field four specific conditions were named in which it should be mandatory: abnormal presentation, operative delivery, bad obstetric history and medical complications.

It was also suggested that services be extended into the home. Pregnancy and childbirth do not occur only in clinics, hospitals and delivery rooms, on ward services and in hospital private rooms. Important aspects take place in the home. We did not say we could do at once all we might like to in the way of home service; but a simple suggestion was advanced that anybody can try out. Why can't the hospitals establish a system of telephone communication with the patient on discharge? Somebody suggested it could even be done before she entered the hospital as a patient. Several agencies are involved. There is perhaps no one plan that would be workable for all—but the basic idea is already working in some hospitals in New York City. Why not in others?

Another topic that was emphasized repeatedly, was prenatal care. Nobody likes it as it is. The doctors are not satisfied with it; the ward attendants are not satisfied with it; nor are those who work in the outpatient departments. Neither the nutritionists nor the nurses—not even the patients—like it. Though nobody used the phrase, we said in effect, "Let's take it out of the basement! Let's give it a new look; let's give it some curtains, some friendliness, some smiles, some decent medical attention." It was felt that organization was needed to do all this and Dr. Hellman said, "Let's give it a director." Why shouldn't we?

How our senior personnel is used, also underwent scrutiny. In the consultation field, for example, and elsewhere in the clinical field, it was questioned whether we are not putting the cart before the horse. The poorest trained person now sees the patient first. If he doesn't know what to do, he goes up the ladder of the hierarchy for help. Maybe we ought to turn the hierarchy around, as in some English hospitals, where the chief of service is the first to see the O.P.D. patient. Why? Because it takes more skill to decide whether or not she really needs expert care. Anyway, we said organization was definitely needed in several places and particularly in the O.P.D.

It was suggested that advice in the use of contraceptive methods might be helpful; and there was discussion of the great opportunity there is for education, for using the time that both the woman and the

staff spend in the prenatal clinic for something more satisfactory to both of them. And—of the utmost importance—someone said there should be an organized anesthesia service in every hospital.

Nutrition should receive more attention. At present, neither knowledge nor practice is adequate on this score. We were even bold enough to say that if a woman didn't have enough nourishment, why didn't we give it to her? We give penicillin to help save lives. Why shouldn't we give the food supplements needed?

We also said, perhaps not loudly enough, that it was extremely important to face up to the obvious shortages in trained personnel. There are not, and there will not be, enough doctors, nurses, social workers, nutritionists, etc., for our increasing population. Let's attack this problem of lack of personnel today, and not wait until the shortages get worse. The National League for Nursing is the only professional group, as far as I know, to have approached this problem realistically.

As Dr. Levine said, if we really knew what caused premature labor and could prevent it, this conference wouldn't be necessary, because premature births are responsible for approximately two-thirds of the total perinatal mortality. Premature babies account for more morbidity, too. Last year it cost the city $360 for hospitalization of the premature baby as against $100 for the full term infant.

To get the answer to this vital question of prematurity, we need to know a great deal more about many specific factors—such as the causes of habitual abortion, the physiology of the uterus, the structure and physiology of the placenta, and the role of nutrition and emotional factors. But here, too, there are things we can start doing now, such as strengthening prenatal care, trying to reach more expectant mothers with better health education, and—as the group discussing this question put it—"avoiding meddlesome obstetrics".

This is one of the few conferences I have attended at which money did not take up most of the discussion time. Somebody said it was necessary; and someone else suggested it might be obtained in part, by extending voluntary hospital insurance to the newborn period. I'm really not worried about this aspect of the problem. In our country, if people have good enough ideas and are well enough organized, the money can always be found to do the job.

We need to decide what we should do and how we are going to do it. That, I think, is the challenge this conference has left us.

THE NEW YORK ACADEMY OF MEDICINE

POSTGRADUATE WEEK 1958

OCTOBER 13-17, inclusive

RESEARCH CONTRIBUTIONS
TO CLINICAL PRACTICE

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Members of the Medical Profession and those working in the allied sciences, are cordially invited to attend all sessions. NO FEE WILL BE CHARGED, but registration for non-Fellows of the Academy will be required.

All inquiries should be addressed to:

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SCIENTIFIC EXHIBIT

October 8-17 (except Saturday and Sunday)

SEE FOLLOWING PAGES FOR PROGRAM

1958 POSTGRADUATE WEEK

TENTATIVE PROGRAM

EVENING LECTURES – 8:30 P.M.

OCTOBER

13th

MEDICAL ASPECTS OF ADVANCES IN MOLECULAR BIOLOGY
Lecturer to be announced

CONTRIBUTIONS OF QUANTITATIVE CYTOCHEMISTRY TO MEDICINE
Lecturer to be announced

14th

HEREDITARY ASPECTS OF DISEASE
Barton Childs, Baltimore, Md.

CONGENITAL DISORDERS OF PLASMA PROTEINS
Charles A. Janeway, Boston, Mass.

HEREDITARY DISEASES OF CONNECTIVE TISSUE
Victor A. McKusick, Baltimore, Md.

15th

THE EFFECT OF ANTIBIOTICS ON MICROBIAL METABOLISM AND RESISTANCE
Lecturer to be announced

OBSERVATIONS ON THE NATURE OF STAPHYLOCOCCAL INFECTIONS
David E. Rogers, New York City

THE CONTROL OF STAPHYLOCOCCAL SEPSIS
Carl W. Walter, Boston, Mass.

16th

PHYSIOLOGY AND METABOLISM OF THE LIVER
Stanley E. Bradley, New York City

METABOLISM AND CONJUGATION OF BILIRUBIN
Irving M. London, New York City

MANAGEMENT OF PORTAL HYPERTENSION
Arthur B. Voorhees, Jr., New York City

(Continued on next page)

17th — THE FATE OF SODIUM AND WATER IN THE RENAL TUBULES
Homer W. Smith, New York City

MECHANISMS OF RENAL TUBULAR TRANSPORT
John V. Taggart, New York City

ELECTRON MICROSCOPY OF THE KIDNEY IN NORMAL AND DISEASED STATES
Johannes A. G. Rhodin, New York City

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PANEL MEETINGS – 3:30 P.M.

OCTOBER

13th — THE DIAGNOSIS AND MANAGEMENT OF CEREBRAL VASCULAR DISEASES
Chairman: Irving S. Wright, New York City

14th — INFLUENZA AND UPPER RESPIRATORY INFECTIONS
Chairman: Walsh McDermott, New York City

15th — GLOMERULONEPHRITIS AND PYELONEPHRITIS
Chairman: William Goldring, New York City

16th — POTASSIUM THERAPY
Chairman: Saul J. Farber, New York City

17th — THE RADIATION HAZARD
Chairman: Joseph E. Rall, Bethesda, Maryland

* * *

SCIENTIFIC EXHIBIT

October 8-17 (except Saturday and Sunday)

Those who have exhibit material appropriate to the subjects included in the Postgraduate Week program are invited to apply for exhibit space. Forms may be obtained by addressing the Secretary, Postgraduate Week, The New York Academy of Medicine, 2 East 103 Street, New York 29, N. Y. Deadline for receipt of applications, *July 1, 1958.*

than capsules containing either the corresponding base or the hydrochloride alone. In addition, the average levels derived from the tetracycline base or the chlortetracycline base were higher than those produced by the corresponding hydrochloride though lower than those resulting from the mixture containing the base and sodium metaphosphate. In the study with chlortetracycline[6] capsules containing a mixture of the hydrochloride and sodium metaphosphate were also included in the crossover, and the average levels produced by these capsules were the same as with the mixture of chlortetracycline base with sodium metaphosphate.

Although the enhancement of blood levels of tetracycline by phosphate, either complexed to the tetracycline or mixed with the base or the hydrochloride, thus seemed fairly well established, some doubts still remained because certain reliable observers (including many whose results have not been published) failed to confirm the findings with the materials and methods they used. Further confusion seemed to be added by a subsequent report of Welch et al.,[7] who, in repeating a crossover study with capsules of tetracycline phosphate complex and tetracycline hydro- chloride with and without sodi- phate, foun[d]

in lower, and sodium metaphosphate in higher, serum antibacterial activity than was observed in their absence. Oil and sorbitol did not interfere with tetra- cycline absorption.

Dicalcium phosphate is widely used as a filler in various capsules, including those of the tetracyclines. The authors cite a large number of other studies that implicate the presence of calcium ions as the cause of the reduced absorption of tetracyclines and show that citric acid can partially neutralize this effect. The depressing effect of food on the serum levels of tetracycline is likewise explained by the goodly amount of minerals contained in commercial laboratory diets, and they postulate that the multivalent cations may be responsible for the poorer absorption of the drug. The authors could not explain the failure of citric acid to enhance serum concentrations when administered with tetracycline base in contrast to its marked effect when given as the hydrochloride. However, they hypothesized that the ability of citric acid to enhance serum levels of tetra- cycline is re- to its ability to form comple- en -available for- be

"...Tetracycline hydrochloride and citric acid, in an encapsulated mixture, produced higher serum concentrations and greater urinary excretions, and hence better absorption of tetracyclines, than any other preparation studied..."

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- dium [illegible] last mentioned paper of et al.[7] indicates that in their study the capsules of tetracycline hydrochloride, chlortetracycline hydrochloride and tetracycline phosphate complex all contained dicalcium phosphate as a filler, whereas the capsules containing citric acid and sodium hexametaphosphate did not contain any dicalcium phosphate. This could clearly explain the discrepancies noted in that study. Likewise, the inconsistencies in other studies may very well have been due to the presence of calcium as fillers in some of the capsules and not in others.

This, however, fails to explain - Welch and Wright,[10] of three capsule- -cycline hy-

were published simultane- with the last mentioned report of Welch et al.[7] These data were based on thoroughly controlled studies both in rats[8] and in man[9] and include additional - -ve to explain, fairly conclusi- -pancies th- have been mer- study -um

[9] Editorial. *The New England Journal of Medicine.* 258:97-99, (January 9) 1958.

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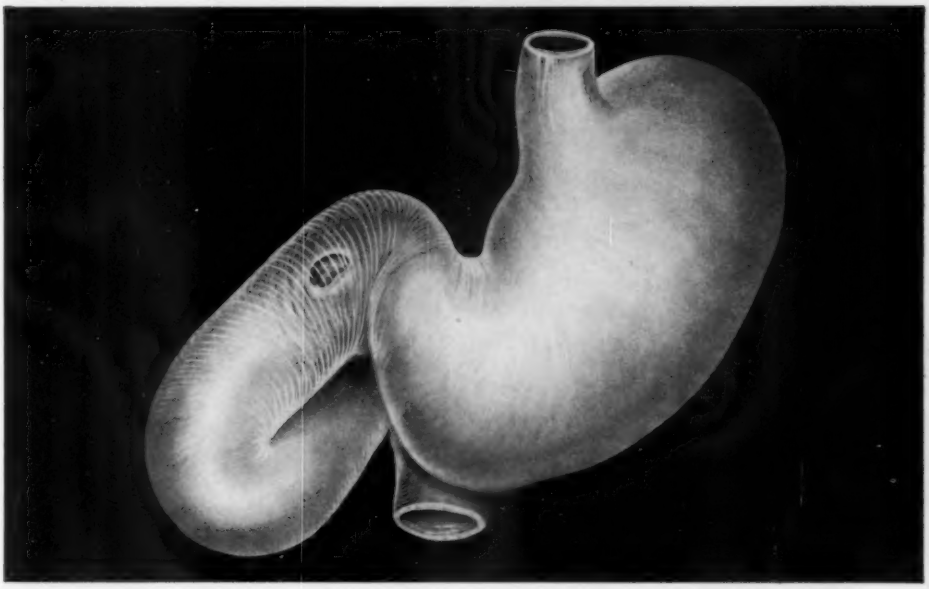

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The average adult oral dosage of Pro-Banthine is one tablet (15 mg.) with meals and two tablets at bedtime.

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*Lichstein, J.; Morehouse, M. G., and Osmon, K. L.: Pro-Banthine in the Treatment of Peptic Ulcer. A Clinical Evaluation with Gastric Secretory, Motility and Gastroscopic Studies. Report of 60 Cases, Am. J. M. Sc. *232*:156 (Aug.) 1956.

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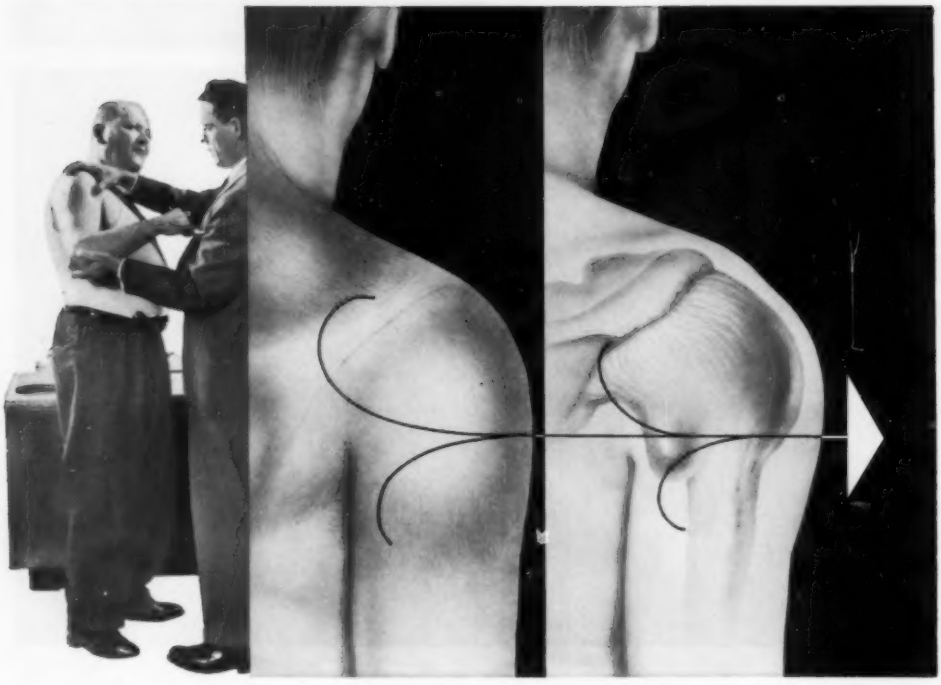
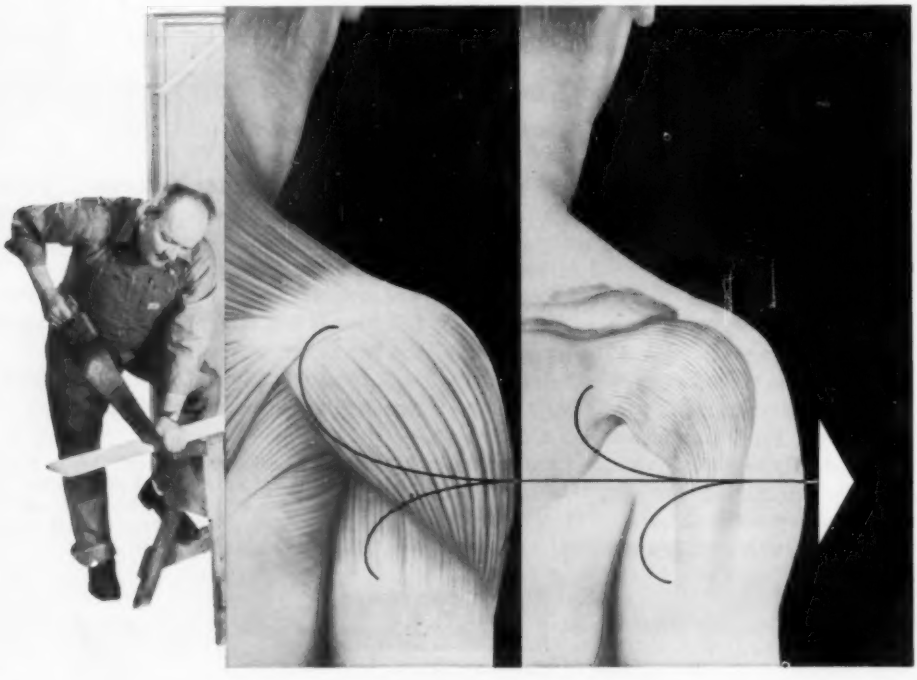


"Rheumatoid arthritis is a constitutional disease with symptoms affecting chiefly joints and muscles."[1] "Pain in the affected joint is accompanied by splinting of the adjacent muscles, with resultant 'muscle spasm.'"[2]



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1. Comroe's Arthritis: Hollander, J. L., p. 149 (Fifth Edition, Lea & Febiger, Philadelphia, Pa. 1953).
2. Merck Manual: Lyght, C. E., p. 1102 (Ninth Edition, Merck & Co., Inc., Rahway, N. J. 1956).

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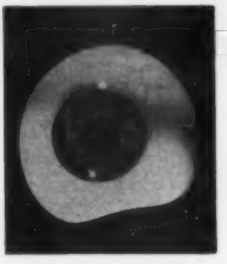

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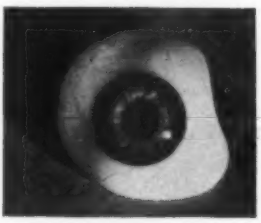

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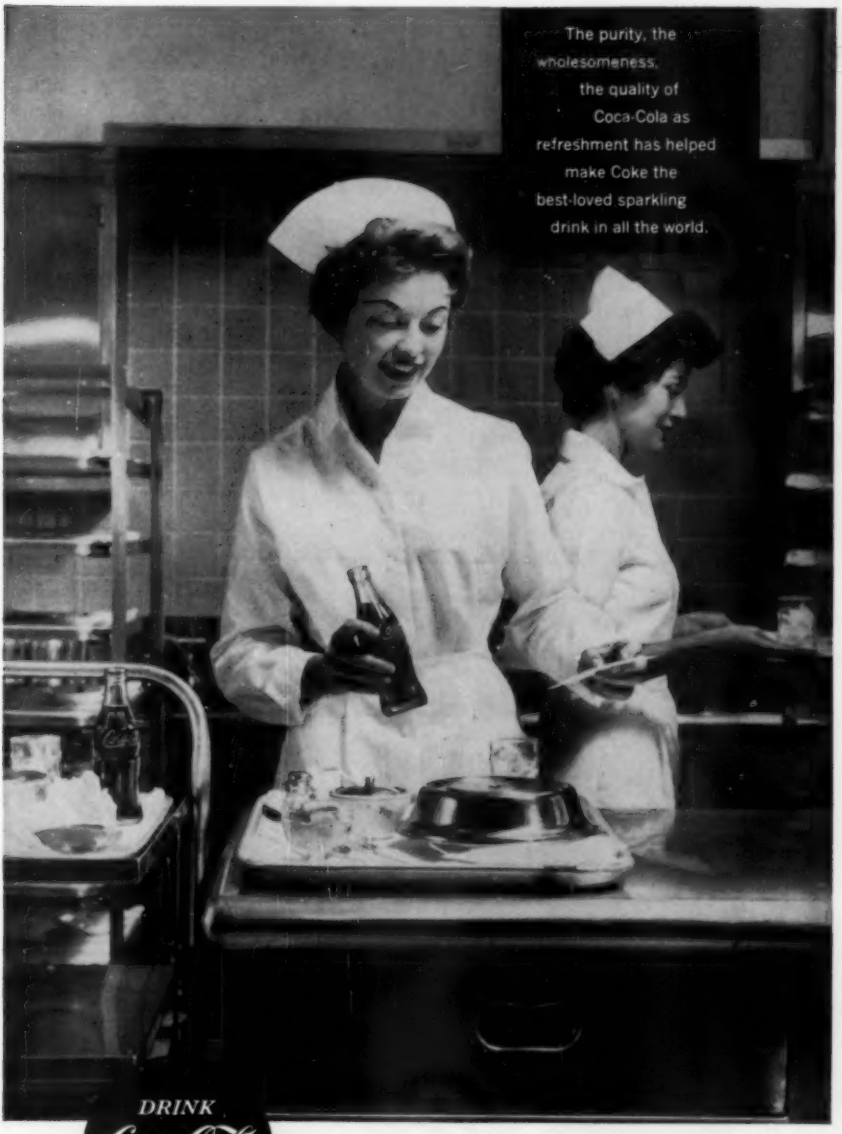
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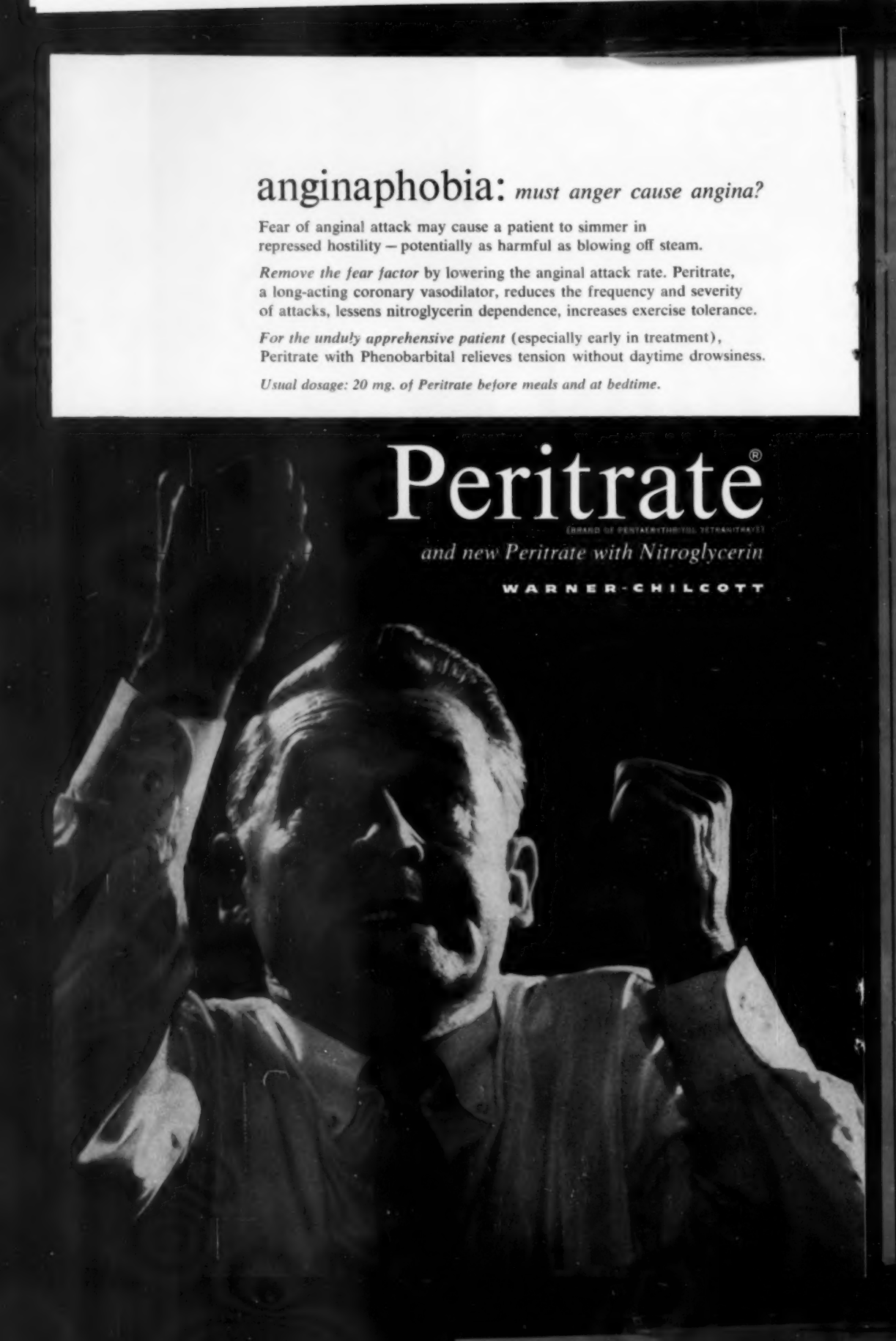

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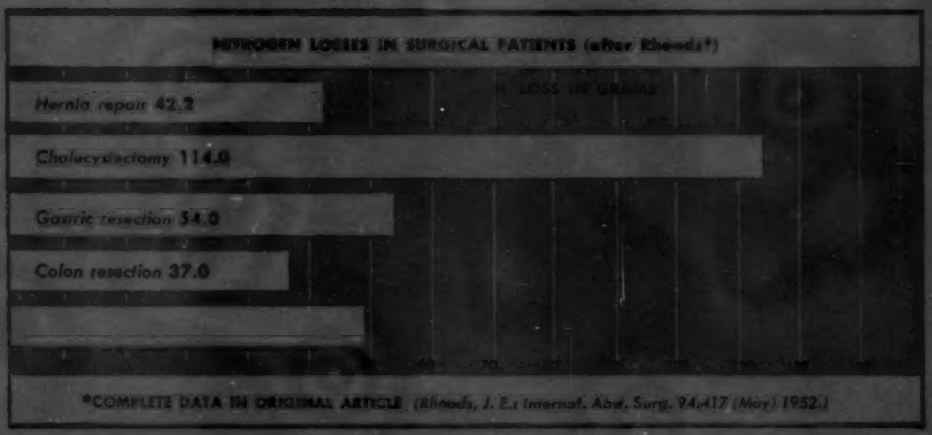
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Patients about to undergo extensive surgery[1] frequently have negative nitrogen balance and protein deficiency. And after any severe trauma, including extensive surgery, the rate of protein breakdown is increased.

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